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INTENSIVE METHODS OF TREATING SYPHILIS

H. N. COLE, M.D.
E. B. HEISEL, M.D.
AND
GEORGE STROUD III, M.D.
CLEVELAND

Paul Ehrlich worked for years synthesizing an arsenical compound to cure syphilis. The therapia magna sterilisans, he thought, had been achieved with his six hundred and sixth preparation, arsphenamine (introduced as salvarsan), to be injected intramuscularly, one injection sufficing. Relapses as well as reactions disclosed differently and he synthesized another arsenical, neoarsphenamine, and later still others. When none of these worked he and his collaborators suggested use of more than one injection. Every physician agreed to the effect of the trivalent arsenical salts on Treponema pallidum, but it required trial and error as well as evaluation of enormous amounts of case material before medicine finally awakened to the profound effect of these compounds on syphilis. Injections of the arsenical were at first widely spaced between other forms of therapy—mercury. Later a physician here and there had the temerity to use injections perhaps once a month, later once a week. It was one of our American dermatologists, Sigmund Pollitzer, who suggested three daily injections of an arsenical followed by a course of mercury, then a rest and repetition of the foregoing. Unfortunately, the worthwhile part of Pollitzer's advice was ignored since his cases relapsed far more frequently than other cases treated in a continuous fashion, the relapse being due to the rest period as we now see it. However, Pollitzer's idea was not forgotten. Quite early the Cooperative Group studies showed that it was not only type of therapy but also amount of therapy given in a continuous manner that played so great a role in "cure." Probably the crystallization of all these studies was the statistical survey of Padgett's [1] indicating the importance in acute syphilis of the number of arsenical injections and conversely the time span in which they were given after inception of the disease.

INTRAVENOUS DRIP THERAPY OF SYPHILIS

A further great stride in syphilotherapy was worked out by Chargin, Hyman, Leifer and their collaborators.[2] They found that when active or inert chemicals, drugs and biologic products are injected intravenously in a rapid manner they may give rise to alarming symptoms, so-called speed shock. On the other hand, by regulating the rate of flow of the preparation by means of an intravenous drip so that not more than 2 to 3 cc. a minute was injected, they were able to introduce even toxic substances like histamine without difficulty. Experiments were then tried on man with like results and Chargin felt that the method might be applied to the use of larger doses of the arsenicals than are ordinarily employed in treating syphilis. First observations were made with neoarsphenamine and results were very promising, but reactions, especially peripheral neuritis and cerebral symptoms, were high and after some ineffectual attempts to use arsphenamine they turned to mapharsen. The dose employed was 240 mg. daily dissolved in 2,000 to 2,400 cc. of 5 per cent dextrose solution administered by the rectal drip. Among 283 patients there were 5 mild cases of peripheral neuritis and, while there were no fatalities from its use, 1 patient developed convulsions two days after termination of therapy and lapsed into a stupor for forty-eight hours. In 2 other cases there were mild cerebral symptoms, all 3 interpreted by them as varying grades of hemorrhagic encephalitis. Therapeutically, of 176 patients followed for at least a year 69 received the full dose of 1,200 mg. and 86 per cent were serologically negative and clinically well. Of another 107 patients receiving less than the full dose of mapharsen for one reason or another, 74 per cent apparently were cured.

Rightfully stimulated by the results, this form of therapy was immediately taken up by other workers in various centers. Thus Dr. D. C. Elliott of the United States Public Health Service reported to Dr. Herbert Rattner [3] of Chicago that more than 1,150 patients had been treated by this method under the auspices of the Middle Western Cooperative Group, and still more recently Dr. R. A. Vonderlehr in a personal note said that some 1,700 patients had received the intravenous drip in a group of midwestern clinics through November

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Read before the one hundred and sixty-second annual meeting of the Massachusetts Medical Society, May 26, 1943, in Boston.

Owing to lack of space, this article has been abbreviated for publication in THE JOURNAL. The complete article appears in the authors' reprints.

From the Department of Dermatology and Syphilology, Western Reserve University School of Medicine, and the Cleveland City, St. Vincent's Charity and University hospitals.

Drs. George Binkley, C. L. Cummer, J. R. Driver, Winthrop Hubler, Max Kraus and C. G. LaRocco gave assistance in completing records as well as in supervising and caring for patients in this study.

Asst. Surg. Gen. R. A. Vonderlehr, Division of Venereal Disease, U. S. P. H. S., and Miss Lida J. Usilton, chief statistician, U. S. P. H. S., gave help and guidance in assembling the material presented in this paper.

1. Padgett, Paul: Long Term Results in the Treatment of Early Syphilis, J. A. M. A. **116:** 7-11 (Jan. 4) 1941.

2. Hirschfeld, Samuel; Hyman, H. T., and Wanger, Justine R.: Influence of Velocity on the Response to Intravenous Injections, Arch. Int. Med. **47:** 284 (Feb.) 1931. Hyman, H. T., and Hirschfeld, Samuel: The Therapeutics of the Intravenous Drip, J. A. M. A. **100:** 305 (Feb. 4) 1933. Hyman, H. T., and Touroff, A. S. W.: Therapeutics of the Intravenous Drip (Further Observations), ibid. **104:** 446 (Feb. 9) 1935. Chargin, Louis; Leifer, William, and Hyman, H. T.: Studies of Velocity and the Response to Intravenous Injections, ibid. **104:** 878 (March 16) 1935. Hyman, H. T.; Chargin, Louis, and Leifer, William: Massive Dose Arsenotherapy of Syphilis by the Intravenous Drip Method: Five Year Observations, Am. J. M. Sc. **197:** 480 (April) 1939. Hyman, H. T.; Chargin, Louis; Rice, J. L., and Leifer, William: Massive Dose Chemotherapy of Early Syphilis by the Intravenous Drip Method, J. A. M. A. **113:** 1208 (Sept. 23) 1939.

3. Rattner, Herbert, and Folk, A. B.: Severe Arsenical Reactions Encountered in the Five Day Treatment for Early Syphilis, J. A. M. A. **118:** 1368 (April 18) 1942. Rattner, Herbert: Personal communication to the authors.

1942 and several hundred more since. Dr. Rattner was one of the earliest to evaluate the possibilities of the technic. He has completed the study of 481 cases at the Cook County Hospital. His technic was above reproach and there were no fatalities, though he did observe an acute glomerulonephritis, anuria, uremia, hepatitis, ileus and pericarditis. There were also 3 cerebral reactions, 2 of them encephalopathy, fortunately all with recovery. Rattner observed 12 to 15 per cent of failures from one five day treatment and he believes this has been materially reduced in his later cases through simultaneous use of soluble bismuth—the latter with no added reactions. Dr. Earl Osborne [4] of Buffalo has thus far treated between 250 and 300 cases, the first 100 prior to Jan. 1, 1942. There was 1 fatality from hemorrhagic encephaltitis in a young healthy girl. There were 2 other near fatalities with recovery, 1 of them a male alcoholic. Dr. Osborne quotes Dr. Udo Wile with having made the keen observation that women either before or during the menstrual period should not be treated with the intravenous drip as at this time the vascular structures would be more affected by a vasculotoxic drug. He states that this was the condition with his patient. He feels that for a large city hospital clientele this is the preferred form of therapy. With other methods two thirds of the patients have absconded before the first year of treatment, whereas at the end of the first year the spinal fluid was not positive in any of his first hundred cases. There have been 2 infectious relapses and 3 serorelapses, a really remarkable result.

Dr. Henry Michelson [5] of Minneapolis, a very careful and skilled clinician, has had two deaths and one near death in 45 cases, making him rather hesitant about intravenous drip therapy. He feels it is too dangerous and that intervals between injections—perhaps with some form of combined fever therapy—is preferable. He leans more to biologic than to chemical therapy.

Drs. Guy and Jacobs [6] of Pittsburgh have treated 21 patients with no ill effects. Dr. Udo J. Wile [7] of Ann Arbor states that he has thus far treated almost 200 cases over a period of two years. There have been no severe reactions and he is favorable to it as the best for rapid treatment procedures.

Dr. Paul O'Leary [8] of Rochester, Minn., has done no work with intravenous drip therapy, feeling that the incidence of serious complications and death was too great. Dr. John Stokes [9] of Philadelphia has done little with it. The personnel problem and setup were difficult for this additional endeavor along with the heavy teaching schedule. Moreover, an aplastic anemia almost in the inception of the work did not help his attitude. They are doing some work with chemotherapy plus fever, using Warren's bath tub technic, but here again the shortage of personnel is difficult. Dr. Charles Dennie [10] of Kansas City, Dr. Joseph Earl Moore [11] of Baltimore and Dr. Dudley Smith [12] of University, Va., have not been using the procedure. Dr. Loren Shaffer [13] of Detroit feels that the five day intensive therapy has a very definite place, particularly for the uncooperative clinic type of patient, but does not think it is universally applicable in all cases of early syphilis. But more in regard to his views later.

Following the report of Baer, Chargin, Hyman, Leifer and others in November 1940 this form of treatment was employed in our City Hospital clinic on 5 patients with early syphilis. They were given daily injections of 1 mg. of mapharsen per pound of body weight for five days. Half of the total dosage was dissolved in 500 cc. of 5 per cent dextrose in distilled water and given by rapid intravenous drip every morning and afternoon. One patient experienced a rather severe headache after the second injection on each of the first three days of therapy. Aside from this there were no reactions.

Three of the patients have been followed for fifteen months or longer. All had strongly positive serologic reactions when the treatment was given. The serologic reactions became negative in from three to five months after the therapy. One was seronegative at fifteen months, another at eighteen months and another at thirty months after completion of the treatment. Two patients were lost from observation. Because of reactions observed in other centers the technic was discontinued for the time, even though we had had no difficulties.

Recently we have treated 5 patients with daily injections of 0.200 to 0.240 Gm. of mapharsen in 2,400 cc. of 5 per cent dextrose in distilled water by slow (twelve hour) intravenous drip for five days. All these patients experienced rather severe phlebalgia. Other than this there were no complications.

In August 1940, moreover, 6 patients with early syphilis were given daily injections of 1 mg. of mapharsen per pound of body weight in 1,000 cc. of 5 per cent dextrose in distilled water by rapid intravenous drip each morning for five days. There were no untoward reactions with this Shaffer technic, which will be described later.

Two patients have been followed for over two years. Both were dark field positive and seropositive when the therapy was given. The serologic reaction on both became negative forty to fifty days after the therapy and remained so twenty-four months later. One, who received a total of 600 mg. of mapharsen, was examined thirty-two months after therapy and found to have strongly positive serologic reactions for syphilis but there were no signs of a secondary relapse. Four patients were lost from observation.

Stimulated by the results from the intravenous drip technic others have adopted a somewhat different technic, the idea in all of them being the introduction of as large and yet safe an amount of trivalent arsenical as the patient with acute syphilis can stand in a limited amount of time.

Thus Schoch and Alexander [14] in Dallas, Texas, have treated over 350 patients. In the beginning they gave twenty daily intravenous injections of 0.060 Gm. of mapharsen. However, the vast majority were treated with ten consecutive daily injections of mapharsen, each 0.120 Gm., the total dosage being 1.200 Gm. There was hemorrhagic encephalitis with death in 1 case and 2 other cases of mild encephalitis with recovery. The only other severe reaction was a case of icterus with recovery. Schoch's reappraisal of a group of 103

4. Osborne, Earl: Personal communication to the authors.
5. Michelson, Henry: Personal communication to the authors.
6. Guy, W. H., and Jacobs, Fred: Personal communication to the authors.
7. Wile, Udo J.: Personal communication to the authors.
8. O'Leary, Paul: Personal communication to the authors.
9. Stokes, John: Personal communication to the authors.
10. Dennie, Charles E.: Personal communication to the authors.
11. Moore, J. E.: Personal communication to the authors.
12. Smith, Dudley: Personal communication to the authors.
13. Shaffer, Loren: Personal communication to the authors.

14. Schoch, A. G., and Alexander, L. J.: Short Term Intensive Arsenotherapy of Early Syphilis: Preliminary Report, Am. J. Syph., Gonor. & Ven. Dis. **25**: 607-609 (Sept.) 1941; Intensive Arsenotherapy of Early Syphilis: Follow-Up Report on the Ten Day Syringe Method of Treatment, Arch. Dermat. & Syph. **46**: 128 (July) 1942.

patients treated with the ten day syringe method, five months after the article was written, showed 83 per cent satisfactory results, 12 per cent failures and 15 per cent still remaining seropositive. They are now using the Eagle technic and think there is a greater margin of safety than with the ten day technic. It is his impression, however, from preliminary results, that they were better with his technic. Time will tell the story. They [15] have since recorded 10 cases of reinfection. Four patients sustained reinfections following orthodox antisyphilitic therapy. The known period of clinical and serologic negativity was four and one-third years for 1 patient and greater than five for 3. Six of the 103 patients noted in the second report sustained reinfections following ten day intensive arsenotherapy for early syphilis (1.2 Gm. of mapharsen). Dark field and quantitative reagin titer findings were furnished to support clinical observations. All the cases were observed by them in both infections and in 1 of them it was believed that there had been three infections in one year. The authors feel that, following intensive arsenotherapy, reinfection is more frequently observed than formerly.

TABLE 1.—*Detroit Plan (Early Cases Only)*

1. Mapharsen (0.05 to 0.07 Gm. according to body weight) three times weekly for twenty doses (six and two-thirds weeks)
2. Bismuth subsalicylate 0.2 Gm. twice weekly for eight doses (four weeks)
3. Mapharsen twice weekly for ten doses (five weeks)

Dr. Loren Shaffer [16] in Detroit tried five daily doses of approximately 1.2 mg. of arsenoxide per pound of body weight administered in 1,000 cc. of 5 per cent dextrose and given by intravenous drip. This required about seventy-five minutes. The maximum daily dose was limited to 0.180 Gm. and the total dose for the course ranged from 0.750 to 0.900 Gm. Some 430 cases have thus far been treated; there have been 2 cases of encephalitis, 1 of them fatal. Later the dosage of arsenoxide was slightly lowered. The incidence of encephalitis was about the same as has been observed with other technics. The incidence of relapses, both clinical and serologic, was somewhat high. In January 1942 an ambulatory intensive method [16] of treatment was adopted by the Detroit Department of Health. It is used only for patients with primary and secondary syphilis who have refused hospitalization for five day treatment or have been considered poor risks. It calls for thirty mapharsen and eight bismuth injections over a period of approximately four months. It is too early to announce results of its use. Dr. Shaffer has been one of the earliest and most vigorous proponents of intensive therapy for early syphilis.

With the Detroit plan (table 1) a spinal fluid examination should be made during the bismuth course or at least on the completion of treatment. After treatment is finished early cases are rechecked at monthly intervals for one year and early latent cases every three months. Thereafter, if negative, both types are checked every six months. Naturally, with early cases a complete physical examination is also in order. If the serologic reaction remains positive for one year, further study is in order.

Shaffer's plan is perhaps somewhat more intensive than the Army plan issued by the Surgeon General of the Army in circular letter 74. Much the same follow-up and routine is used in the Army plan as with the Shaffer Detroit plan.

The Army plan (table 2) calls for forty mapharsen and sixteen bismuth injections in a period of twenty-six weeks.

Shaffer is already disappointed with the Detroit plan because of the high percentage of patients lapsing therapy. Consequently he thinks the five day hospital plan is preferable, though it is hardly suitable to all cases and must be carried out by expert personnel. He thinks that, until more experience can be gained, when one is dealing with the ordinary run of mine clinic patient, who is none too cooperative, either the Army plan or the Detroit plan should be adopted for general use.

Dr. A. B. Cannon [17] of the Vanderbilt Clinic in New York still has great faith in arsphenamine, and since July 1941 he has completed the treatment of 226 persons. The patients are hospitalized and of the 189 whom they have been able to follow 123 had negative serologic tests within a period of two weeks to one year, the average being three and one-half months. The plan of treatment has been changed four different times. The present one necessitates four daily intravenous injections of arsphenamine in concentrated form. The total dosage runs from 3.0 Gm. minimum to 3.6 Gm. maximum. Patients are started on large doses, getting almost half of their treatment in the first two days. There have been 2 cases of encephalitis, with survival in both, 2 of moderate neuritis and 3 cases of icterus, 1 of them a toxic hepatitis. There have been twenty-five mucorecurrences and two persisting serologic reactions.

Eagle and Hogan undoubtedly correctly approached the treatment of early syphilis by the experimental route,

TABLE 2.—*Army Plan (For Early and Latent Cases)*

	Mapharsen		Bismuth
Week 1		Week 1	
2		2	Bismuth subsalicylate
3		3	0.2 Gm. intramuscularly
4	Mapharsen intravenously	4	once weekly, 5 doses
5	0.05 to 0.07 Gm. adjusted	5	
6	to weight twice weekly for		
7	10 weeks; total 20 injections		
8			
9			
10			
11		11	
12		12	
13	Omit mapharsen	13	Bismuth as above, once
14	6 weeks	14	weekly for 6 doses
15		15	
16		16	
17			
18			
19			
20			
21	Mapharsen as in first		
22	course twice weekly; total	22	
23	20 injections	23	Bismuth as above,
24		24	once weekly for
25		25	5 doses
26		26	

working with rabbit syphilis. It would be impossible in this paper to review all the work they have done.[18] While rabbit syphilis is not necessarily human syphilis, a great number of the truths applicable to the one will

15. Schoch, A. G., and Alexander, L. J.: Reinfection in Syphilis, Am. J. Syph., Gonor. & Ven. Dis. **27**: 15 (Jan.) 1943.
16. Shaffer, Loren W., and Salchow, P. T.: Report of Social Hygiene Division, Detroit Department of Health, September 1942.
17. Cannon, A. B.: Personal communication to the authors.
18. Eagle, Harry, and Hogan, R. B.: The Intravenous Drip and Other Intensive Methods for the Treatment of Syphilis, Science **95**: 360 (April 3) 1942. Eagle, Harry; Hogan, R. B., and Kemp, J. E.: The Importance of the Time Factor on the Evaluation of "Cure" in Syphilitic Rabbits, Am. J. Syph., Gonor. & Ven. Dis. **26**: 557 (Sept.) 1942. Eagle, Harry, and Hogan, R. B.: An Experimental Evaluation of Intensive Methods for the Treatment of Early Syphilis: I. Toxicity and Excretion, Ven. Dis. Inform. **24**: 33 (Feb.) 1943; An Experimental Evaluation of Intensive Methods for the Treatment of Early Syphilis: II. Therapeutic Efficacy and Margin of Safety, ibid. **24**: 69 (March) 1943.

apply with the other and vice versa. One very important item that they have brought out is with regard to "cure" in rabbit syphilis. They find that "until time limits within which infectious relapse may occur in the rabbit have been more clearly defined the absolute curative dose of arsenicals in rabbit syphilis cannot be determined by lymph node transfer. . . . Even data as to the relative efficacy of various treatment procedures must be interpreted in the light of the time allowed to elapse between treatment and the following lymph node transfer." Their study showed that six months after treatment in a large series of rabbits, apparently cured at three months as judged by node transfer, 37 per cent of them were still infectious. Apparently the disease was actually quiescent at three months after treatment but not cured. Is there a lesson for us in this in considering human syphilitic therapy? They find in rabbit syphilis that the time factor has much to do in determining the toxicity of a treatment system. Thus the same treatment of syphilis may be intensified; the treatment period may be shortened by various methods, but they have definite and predictable effects on the margin of safety. In the short term intravenous drip, treatment is concentrated within a few days but the mapharsen is given in a continuous slow infusion for many hours daily. Such a slow infusion is less toxic than single daily syringe injections of the same amount of mapharsen; but it is only slightly less toxic than multiple syringe injections (e. g. four times daily) distributed over the same time period. Moreover, in rabbits the therapeutic efficacy of mapharsen given by slow intravenous drip was usually less than if the same amount of the drug was given by repeated syringe injections, whether triweekly, daily or four times daily. Another method of intensifying treatment is to give the same number of injections but at shorter intervals. Thus, instead of twenty weekly injections one may give injections three times weekly for seven weeks, daily for twenty days or twice daily for ten days. It is clear that, the shorter the time interval between injections, the more pronounced will be their cumulative toxicity. The intravenous drip was significantly less effective than multiple syringe injections administered over the same time period in rabbit syphilis. An appreciable condensation of treatment beyond that permitted by triweekly, daily or multiple daily injections can be accomplished only at the cost of safety by an arbitrary decrease in the total number of injections.

Eagle and Hogan have suggested a clinical adaptation of their studies in human beings with early syphilis. The patients are given a weekly intramuscular injection of bismuth subsalicylate 0.2 Gm. and triweekly intravenous injections of mapharsen for six, eight, ten or twelve weeks. Thus far, March 5, between 1,900 and 2,000 patients have been treated at various cooperating clinics throughout the country. In the Cleveland area we have treated the patients at the University Hospital and Charity Hospital with the eight week method and at the Cleveland City Hospital with the ten week method. Naturally it is too early to evaluate the results of this therapy, though it appears to be quite promising. The great difficulty has been to keep the patients on regular treatment. At the first two institutions a total of 114 patients have thus far been treated and at the City Hospital a further 95, of whom 107 have completed their course of treatment. Of these 22 missed no treatments, 34 missed one to five treatment days, 20 missed six to ten treatment days and 31 over ten treatment days, a total of 107 patients. Unfortunately 34, or 16.2 per cent, have already been lost from observation or treatment; fortunately, 11 of these were after completion of therapy, but this does not help future evaluation of the data. Moreover, in 12 of the cases under the eight week regimen and in 12 under the ten week regimen it has been necessary to discontinue the treatment because of reactions. Seventeen were much alike, characterized by nausea, vomiting, general malaise, photophobia, chills and fever from 39 to 40 C. (102.2 to 104 F.). Shortly after onset of the symptoms the patients showed some conjunctival injection and edema of the face. These symptoms came on after the fifth or sixth injection and from nine to twelve days after the first injection of mapharsen. One patient developed an icterus lasting fifteen days. Another patient after the fifth injection developed a daily asymptomatic, spiking temperature to 39.5 C. (103 F.). He was found to have moderately far advanced pulmonary tuberculosis. Following this case a preliminary chest plate was taken in all cases on intensive therapy.

To illustrate what we speak of as our "fever-conjunctival injection-facial edema syndrome":

A Negro woman with early mucocutaneous syphilis was started on intensive therapy on July 9, 1942. After the fifth injection of 0.06 Gm. of mapharsen she had a slight headache. Several hours after the sixth injection of mapharsen she developed nausea and vomiting followed by circumocular edema, conjunctival suffusion, headache, weakness and fever of 39 C. (102.2 F.). It then took five days for her fever to subside. A week after onset of this reaction she received 0.01 Gm. of mapharsen with immediate recurrence of the previous symptoms. Twelve days after this reaction 0.1 Gm. of neoarsphenamine intravenously produced the same reaction and, in addition, profound muscular weakness. She recovered from this fairly well over the period of a week. Subsequently she received eight injections of iodobismitol every week. Three months after the original reaction 0.01 Gm. of mapharsen produced no untoward result. A few days later she moved to Kansas and has not been heard from since.

There has been one relapse at City Hospital, mucocutaneous in type, in a woman who during the course of treatment missed thirteen treatment days. There was also one in a woman under the eight week regimen. She also had missed twenty-four treatment days.

There is a further meningitic type of relapse:

A man aged 57, an Italian, was seen with a chancre and early mucocutaneous syphilis which was dark field positive. At the beginning of therapy on July 16, 1943 his Wassermann and Kline reactions were 4 plus. He then received regular therapy for eight weeks with the exception of one visit, which he lapsed. At the completion of therapy his Wassermann reaction was 4 plus, Kline diagnostic 1 plus and Kline exclusion 3 plus. Six weeks after therapy his Wassermann reaction was 1 plus, Kline diagnostic negative and exclusion 2 plus. Two months after therapy his Kline diagnostic and exclusion reactions were negative. Seven weeks after therapy his spinal fluid showed 300 cells, positive Ross-Jones, 432110 colloidal mastic curve and 4 plus Wassermann reaction in 0.5 and 1.0 cc.

FEVER THERAPY IN SYPHILIS

We now come to another milestone in the therapy of syphilis—fever treatment. Wagner Jauregg was the first to use a form of hyperthermia, malaria, for treating dementia paralytica. Later this treatment was tried in early syphilis and found to be unsuccessful. From malaria therapy we have drifted to the use of other fever producing implements, foreign protein therapy, e. g. typhoid-paratyphoid intravenous injections, hot baths, the inductotherm and the hypertherm. Their

value in central nervous system syphilis is unquestioned, and investigators have naturally turned to them in the treatment of early syphilis. It was an American dermatologist, J. F. Schamberg,[19] who as long ago as 1926 reported the beneficial effects of hot baths in experimental rabbit syphilis. In 1935 Epstein and Cohen [20] and in 1936 Neymann, Lawless and Osborne [21] found such treatment to be ineffective in human syphilis. This has been confirmed by Boak, Carpenter, Jones, Kampmeier, McCann, Warren and Williams [22] and by Simpson, Rose and Kendall.[23] However, when this fever therapy is combined with chemotherapy it may be a different story. The interested reader may consult the recent review of Simpson, Kendell and Rose.[24] These authors [24] have a group of *27* patients with early syphilis observed for four to eight years who have had no clinical or serologic relapse. They received fever therapy consisting of either twelve three hour or ten five hour sessions (rectal temperature 105 to 106 F.) administered once or twice weekly. With each treatment an arsenical preparation (neoarsphenamine 0.3 Gm. or mapharsen 0.04 Gm.) and a bismuth compound (containing 0.2 Gm. of metallic bismuth) were administered. Following the fever therapy, injections of the chemotherapeutic agents were continued for an additional twenty weeks, injections of the arsenic and bismuth being concurrent. They further report on a series of 23 patients observed from six months to two and one-half years. The patients were given a preliminary injection of 0.25 Gm. of bismuth subsalicylate, then placed in a hypertherm and given a ten hour session of artificial fever at 106 F. Mapharsen was used in all the cases. Two patients received 240 mg. by intravenous drip during the period of fever at 106 F. This was abandoned in favor of administration of injection by the syringe method in 60 mg. doses at intervals of three hours. Six patients were given two injections (120 mg.), five received three injections (180 mg.) and 3 received four injections (160 mg.). The first injection was given when the rectal temperature first reached 106 F., the second at the end of the third hour, the third at the end of the sixth hour and the fourth at the end of the ninth hour. No other treatment was given. Serologic reversal was dependent on the height of the initial pretreatment titer. It occurred in from twenty-one to one hundred and seventy-six days. The authors state that the number of patients is small and the period of observation insufficient to permit adequate clinical evaluation. They believe, however, that the results are sufficient to justify further investigation. There can be little doubt about the value of their observations, and they are to be congratulated on their conservative approach. As we understand it, a quite similar procedure is being carried on by Dr. Nathaniel Jones and S. L. Warren [25] at the Duval County Hospital, Jacksonville, Fla., where they have treated well over 100 cases, and at the Chicago Intensive Treatment Center under the direction of Dr. H. Worley Kendell,[26] where they have in a period from October 1942 to date treated a total of 350 or 400 patients. At the latter institution treatment consists in eight hours of fever at 105.6 to 106 F. and there is given arbitrarily to men 0.090 Gm. of mapharsen and to women 0.060 Gm. One third of the mapharsen is given when the temperature reaches its height and one third at approximately three hours and six hours afterward. They also administer 1.5 cc. of 10 per cent suspension of bismuth subsalicylate before treatment is started in the morning. Dr. Kendell furnished the information thus far available and urges extreme conservatism until sufficient material has been treated and carefully evaluated. He is quite emphatic that their work is still in the experimental stage. They plan on gradually increasing the dosage.

THE COMBINED SYRINGE METHOD THERAPY PLUS FEVER

In 1937 Thomas and Wexler in New York City [27] increased the number of injections of mapharsen from one to two a week and by 1938 to three a week for four weeks for all patients with early infectious syphilis. In the light of the intensive therapy they determined to attempt rapid massive treatment without the continuous drip—their facilities at Bellevue did not easily allow the latter. Later they stepped up their dosage still further, using the standard syringe method for injection, giving at first 0.060 Gm. of mapharsen twice daily for ten days, the same dose, 1.200 Gm., used by the Mount Sinai group. Later they tried 0.100 Gm. twice daily, which worked nicely until the 111th patient, who had a fatal encephalitis. Since then they have endeavored to keep the total dosage of mapharsen under 0.800 Gm. in a period of ten days. Dr. Thomas feels, however, that such a dosage to be therapeutically effective must be supplemented with fever. He states that the program they have used now for six months and which is quite satisfactory consists of ten daily injections of mapharsen 0.060 Gm. each with four fevers induced by typhoid vaccine. The fevers are given as a rule on the second, fourth, sixth and eighth days. The dosage is varied somewhat according to weight. Originally Thomas felt that fever prevented toxic reactions [28] of arsenical drugs. He later reversed this opinion.[29] Dr. Thomas thinks that intravenous drip therapy has no advantage over the syringe technic and certainly their results are even as good. Intravenous drip therapy is also probably more toxic. He has also treated 50 patients with Eagle and Hogan's three injections of mapharsen a week for six or eight weeks. He thinks the treatment is therapeutically effective but that it is a most unsatisfactory plan and unpractical in their work, in which they have so many Negroes and irresponsible patients. To this we heartily agree. All their work has been most painstaking, very carefully planned and carried through and presents a most convincing argument in favor of the syringe technic plus fever treatment.

19. Schamberg, J. F., and Rule, Anna: Studies of the Therapeutic Effect of Fever in Experimental Rabbit Syphilis, Arch. Dermat. & Syph. **13:** 243 (Sept.) 1926.

20. Epstein, N. N., and Cohen, Maurice: The Effects of Hyperpyrexia Produced by Radiant Heat in Early Syphilis, J. A. M. A. **104:** 883 (March 16) 1935.

21. Neymann, C. A.; Lawless, T. K., and Osborne, S. L.: The Treatment of Early Syphilis with Electropyrexia, J. A. M. A. **107:** 194 (July 18) 1936.

22. Boak, Ruth A.; Carpenter, C. M.; Jones, Nathaniel; Kampmeier, R. H.; McCann, W. S.; Warren, S. L., and Williams, J. R., Jr.: The Inadequacy of a Single Prolonged Fever for the Treatment of Early Acute Syphilis, Am. J. Syph., Gonor. & Ven. Dis. **26:** 291 (May) 1942.

23. Simpson, Walter M.; Kendell, H. Worley, and Rose, Donald I.: Quantitative Serologic Studies in Early Syphilis: I. Treatment with Artificial Fever Alone, II. Treatment with Artificial Fever Combined with Chemotherapy, III. Treatment with a Single Intensive Session of Combined Fever-Chemotherapy, Ven. Dis. Inform. **23:** 403-415 (Nov.) 1942.

24. Simpson, W. M.; Kendell, H. W., and Rose, Donald: Developments in the Treatment of Syphilis with Artificial Fever Therapy Combined with Chemotherapy During the Past Decade, Brit. J. Ven. Dis. **17:** 1 (Jan.-April) 1941.

25. Jones, Nathaniel, and Warren, S. L.: Personal communication from Dr. R. A. Vonderlehr.

26. Kendell, H. Worley: Personal communication to the authors.

27. Thomas, E. W.; Wexler, Gertrude, and Dattner, Bernhard: Cerebral Reactions Associated with Massive Mapharsen Treatment of Early Syphilis, Am. J. Syph., Gonor. & Ven. Dis. **26:** 529 (Sept.) 1942. Thomas and Wexler.[28] Thomas.[29]

28. Thomas, E. W., and Wexler, Gertrude: Treatment of Early Syphilis with Rapid Injections of Mapharsen, Am. J. Pub. Health **31:** 545 (June) 1941.

29. Thomas, E. W.: Personal communication to the authors.

COMMENT

It is fair to say that from the data given here evidence is presented showing that early syphilis is being cured by intensive treatment methods, whether it be intravenous drip, the syringe technic, multiple injections of Eagle, or fever therapy and intravenous drip or syringe treatment plus fever. The patients are not only cured but, as Schoch and Alexander show, they are even being reinfected in appreciable numbers.

Stokes [30] has recently reviewed the difficult problem. He points out that a new system of treatment of syphilis must equal or surpass the curative expectancy of the older ones, lead to less infectious relapses, cure more mothers and protect more children and lessen the incidence of cardiovascular and central nervous system syphilis. On the other hand, when we talk about the relatively benign character of much early syphilis, 40 to 50 per cent, and the fact that with relatively small amounts of treatment, if it doesn't disturb the defense mechanism, this may even be raised to as high as 70 per cent, here we are completely ignoring the public health problem of syphilis, especially in wartime. He quite properly insists that evaluation of a system of treatment requires two to four years as far as relapse is concerned and ten years for evidence of progression. A new sytem must be cheap and rapid, control the lapse problem and allow treatment of more persons per unit of time, personnel and equipment. All these arguments are, of course, in favor of intensive methods though, as Stokes notes, the man cured with intravenous drip or with fever plus chemotherapy must be followed afterward even as much as his lady friend treated by the longer but safer eighteen months method. And too he states that with intensive methods wherein patients are even paid for follow-up visits the loss rate is 17 per cent and in some clinics 6 to 20 per cent up to six months. He thinks that long term treatment in the modern syphilis clinic is carried through in 25 per cent of the early cases and 50 per cent ultimately receive satisfactory irregular treatment. Moreover, that in really good clinics with effective case holdings it may be raised to 50 per cent with 70 to 80 per cent ultimately receiving satisfactory irregular treatment. In this connection one should remember that we are not dealing with a half dozen top clinics but with the run of mine clinic throughout the United States. How well is this clinic holding its cases? It is not necessary to answer: the record is bad, spelled with a capital B. He is probably right in his contention that the percentage of relapse is about the same with intensive methods as with conventional treatment. We agree that for the present, at least, intensive therapy should be reserved for relatively acute syphilis—not later than early latent.

We now come to the real problem with intensive methods. Stokes says that for 4,871 patients treated with all the intensive methods there was a mortality of 1 : 220 and a morbidity of nonfatal encephalitis of 1 : 160. Shaffer makes the figure for mortality 0.3 per cent. It is true that with older methods encephalopathy is very rare; he puts it 1 : 20,000. He also adds that deaths from mapharsen are thus far only 6 after administration of millions of doses. He thinks that the death rate is probably one hundred to two hundred times that from older methods. In reply to this we must add the ultimate mortality or morbidity of an enormous number of early uncooperative syphilitic patients who take a few treatments and lapse. And, too, how many new infections do they pass on and thus keep the syphilitic ball rolling? How many mothers and how many babies are infected by them before their disease gets so old that it is no longer transmissible? Moreover, would not such an intensive technic be a partial answer to our expert help problem in our clinics? The patient receives his treatment and then is through except for follow-up and occasional examinations.

Vonderlehr and Usilton [31] have recently analyzed the 1,895,778 serologic reports of men aged 21 to 35 who were examined under the Selective Service Act of 1940. The rate of prevalence of syphilis among the entire male population between 21 and 35 is estimated to be 47.7 per thousand. However, the rate of prevalence among Negro selectees is 253.3 per thousand and among white selectees 17.4 per thousand. Moreover, if one turns to urban centers in the South it is found that the rate of prevalence among Negro men ran 413 per thousand in Florida, 407 in Georgia, 358 in Arkansas, 339 in Maryland, 431 in Mississippi, 384 in Texas, 417 in South Carolina, and so on. Unfortunately, these data present the crux of the whole syphilis problem. The rate of prevalence is highest among the most ignorant and least cooperative part of our population. In the Cleveland district it is just this portion of our patients that are hardest to hold, that are easiest lost, in fact so effectually that even their draft boards cannot find them. The common complaint from all workers in syphilotherapy is difficulty in holding the uncooperative patient. A few treatments and he is gone.

With those forms of treatment in which the patient is hospitalized and receives his full complement we are at least sure that he or she has this under his or her skin. True, a certain number will relapse, but this is a small number compared to the number lost under any routine form of treatment. Moreover, we are in the midst of a world war in which public health problems, especially regarding syphilis, are paramount. It is our opinion that at least for the duration all such uncooperative patients with early syphilitis as come to our public health clinics should be hospitalized and treated by intensive methods, i. e. the intravenous drip, the Schoch method, the hypertherm treatment plus intravenous medication or by the Thomas and Wexler method. Stokes thinks the future should look to the multiple dose technic of Eagle and Hogan or to a combination of two or three sharp prolonged pyrexial rises with massive dose mapharsen therapy by drip or multiple injections. For such patients as are seen in our clinics the answer, in our opinion, is not to be found in the Eagle technic—the patient must be hospitalized and treated while we have him and for that reason the Thomas and Wexler technic with daily injections of mapharsen 0.060 Gm. plus intravenous typhoid-paratyphoid on the second, fourth, sixth and eighth days, the five day intravenous drip perhaps with added soluble bismuth intramuscularly, or the hypertherm plus intravenous chemotherapy are preferable. It stands to reason that such therapy should be administered only by experts in the field, trained to meet any emergency. Attempts at this type of therapy by the tyro can only lead to disaster. Moreover, such therapy requires a competent house staff and nursing staff skilled in handling such cases. The next few years are going to do much in answering this great problem—the intensive therapy of syphilis. And, apparently, American medicine is at the fore in handling this grave question.

30. Stokes, John: The Wartime Control of Venereal Disease, J. A. M. A. **120**: 1093 (Dec. 5) 1942.

31. Vonderlehr, R. A., and Usilton, Lida J.: Syphilis Among Men of Draft Age in the United States, J. A. M. A. **120**: 1369 (Dec. 26) 1942.

THE SYNTHETIC ESTROGEN OCTOFOLLIN (IN OIL)

REPORT OF CLINICAL INVESTIGATION

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Although there is no doubt concerning the efficacy of estrogen therapy in the female climacteric, there is considerable uncertainty about the optimal preparation to be used. The criteria for effective treatment are two: subjective relief and vaginal smear response. To the practitioner interested primarily in the welfare of his patients the relief of symptoms is of more importance, and rightly so, than the results of any objective tests which may be made. Until such time as some investigator has at his disposal a group of young women from whom all ovarian tissue has been removed by surgical means, evaluation of the activity of estrogens in human therapy by the vaginal smear technic can never be a precise laboratory procedure. It is true, of course, that some estimate of the degree of response to the therapy can be gained by the smear technic, and we have used such tests to supplement our subjective findings. In choosing an estrogen the physician must consider also other factors—cost (to him or to the patient) of adequate therapy and the extent to which toxicities or side reactions occur following oral or parenteral therapy.

There would seem to be nothing to be gained by a lengthy discussion here of the voluminous literature representing the experiences of investigators and clinicians with diethylstilbestrol. The report of the Council on Pharmacy and Chemistry [1] together with the review articles mentioned therein must be familiar to all workers in the field. It would appear to be universally accepted that diethylstilbestrol is a remarkably effective estrogenic drug when administered either orally or parenterally. There has been considerable controversy, however, over the degree to which toxicities or side reactions are manifest during the administration of this synthetic estrogen.

During the last year I have been using a new synthetic estrogen, octofollin,[2] on a large group of climacteric patients. This compound, which is not a derivative of stilbestrol, has the chemical name 2-4-di(para-hydroxyphenyl)-3-ethyl hexane. The steps leading to the development of this compound have been outlined by Blanchard, Stuart and Tallman,[3] and reports of the physiologic studies of this estrogen were presented in 1942 from the same laboratory.[4] Freed and his co-workers,[5] and Greenhill [6] reported satisfactory results with this compound in menopausal patients and indicated that it was much less toxic than stilbestrol or hexestrol. Murphy [7] reported that satisfactory results have been obtained with the use of octofollin in the relief of the symptoms of the menopause, in gonorrheal vaginitis in children and in the suppression of lactation. Jaeger and his co-workers [8] mentioned its use in gonorrheal vaginitis and believed it to be a most efficient estrogen.

EXPERIMENTAL MATERIAL AND RESULTS

It was my intention at the outset to test the efficacy of octofollin both by oral and by parenteral administration. At the start, the memory of side reactions with stilbestrol therapy resulted in overcaution in the oral administration of this new synthetic, and as a consequence the clinical response was not encouraging. However, not one of the patients reported any untoward reaction of any kind during the course of therapy. The average daily dose by mouth in this series of patients was 1.0 mg. Therapy with octofollin in oil was begun by deep intramuscular injection and the results were very satisfactory. In all the cases to be reported here the estrogen was administered by this route. Therapy was given to a series of 21 women with various symptoms indicative of estrogen deficiency. The summary of the results on these cases, giving dosage data, is given in the accompanying table. Not one of these patients ever demonstrated any toxic symptoms or local reaction at the site of injection. Gastrointestinal disturbances which were not at all uncommon with diethylstilbestrol were absent, and there was no evidence of pelvic pain or discomfort, no vaginal bleeding during therapy and no dermatitis. The amount and frequency of the dosage are determined by the type of patient and the severity of the symptoms.

The cases in this series ranged from mild menopause types to those with the more severe symptoms of the surgical menopause. The majority of the patients had similar symptoms with an average degree of severity.

In the accompanying table the five starred patients had liver function tests. Four of these showed completely normal function both before and after considerable therapy. The fifth patient, D. M., having latent syphilis and chronic cholecystitis, exhibited a 2 plus cephalin flocculation test at the beginning of therapy and there was no change following six months of octofollin therapy.

Vaginal smears were done on all the patients shown in the table. I have been using the iodine staining reaction as a measure of estrogen response. In the majority of cases there was a moderate to pronounced reduction in the number of iodophilic cells before therapy. Following therapy there was an improvement in the appearance of the smear in almost all cases, although complete cornification was observed in but 2 cases. It is quite apparent that definite, or complete, relief of menopausal symptoms can follow estrogen therapy without the necessity of producing completely cornified vaginal smears.

Space does not permit the insertion of detailed protocols on all the patients. One typical protocol is given here, however, with the idea that it will give a better idea of the way in which treatment was carried out on the average patient:

E. W., white, aged 44, except for a sacroiliac strain and some hypertrophic arthritis of the sacroiliac joint, had no illness or operation. When first seen in October 1941 the patient complained of low backache, also spells of hot flashes and vertigo, exhaustion and at times some precordial discomfort. The physical and x-ray examination revealed no serious pathologic condition; however, there was some moderate hypertrophic reaction of the right sacroiliac joint. The Kahn reaction, blood count and urinalysis were essentially negative. Liver function tests

1. Diethylstilbestrol, Report of Council on Pharmacy and Chemistry, J. A. M. A. **119**: 632 (June 20) 1942.
2. Octofollin is a development of the Research Laboratories of Schieffelin & Company, New York, and was supplied through the courtesy of Dr. E. W. Blanchard of that organization.
3. Blanchard, E. W.; Stuart, A. H., and Tallman, R. C.: Endocrinology, to be published.
4. Blanchard, E. W.: Endocrinology **30**: S1026 (June) 1942. Stebbins, A. B., and Blanchard, E. W., ibid. **30**: S1041 (June) 1942.
5. Freed, S. C.; Eisin, W. M., and Greenhill, J. P.: J. Clin. Endocrinol. **2**: 213 (April) 1942.
6. Greenhill, J. P.: Am. J. Obst. & Gynec. **44**: 475 (Sept.) 1942.
7. Murphy, J. A.: Am. J. Obst. & Gynec., to be published.
8. Jaeger, A. S.; Moenning, W. P., and Bowman, G. W.: Urol. & Cutan. Rev. **47**: 81 (Feb.) 1943.

were made. The cephalin-cholesterol and bromsulphalein tests were negative, and four weeks after the use of the synthetic estrogen octofollin the tests still showed completely normal liver function. The menstrual history was normal. In the past six months the periods had been growing more scanty and becoming a little irregular. Vaginal examination showed a perfectly normal cervix and fundus and no evidence of tumors or inflammation. The vaginal smears revealed quite a few round or oval atrophy cells.

The patient received therapy of natural estrogenic hormone 10,000 international units parenterally twice a week for six injections. This was followed by a definite symptomatic improvement for four or five weeks. The vaginal smears made during the time of greatest improvement showed little cornification with the atrophy cells still present to a moderate degree, notwithstanding the subsidence of clinical symptoms. With the return of symptoms such as hot flashes and vertigo the patient was placed on diethylstilbestrol orally 0.5 mg. per day. The symptoms subsided within a few days, but the patient became nauseated and had a sense of soreness and fulness of the breasts after eight days, so that it became necessary to discontinue the therapy. The injection of diethylstilbestrol 0.5 mg. twice a week also gave clinical improvement but also created the toxic symptoms as before and was discontinued.

In May 1942 the patient was placed on injections of the synthetic estrogen octofollin, receiving 2 mg. twice a week for one month without there being the least sign of toxic symptoms. She received thereafter 5 mg. a week and later every two weeks for two months more. Complete relief of hot flashes, sweats and dizziness resulted and the patient generally was better after the fourth injection. This improvement continued for over six months without further injection and with no return of symptoms. An apparent improvement in the arthritic condition was also reported by the patient.

The hypertension which seems to be present in certain menopause patients seemed also to be improved with octofollin therapy. This is particularly noted in one patient, M. L. M. in the table, whose blood pressure before the start of treatment varied between 180/110 and 200/120. After three months of therapy the blood pressure was 150/90 to 160/98. Similar decreases in blood pressure, though less striking, were noted in other patients in this series.

COMMENT AND CONCLUSIONS

Octofollin in my experience provides prolonged beneficial effects. This means sustained as well as additional comfort for the menopausal patient.

Undesirable side reactions, such as headache, nausea, vomiting, dizziness, soreness of the breasts, pelvic pain and excessive or frequent uterine bleeding, were not encountered in my experience. Such reactions were encountered frequently in therapy with diethylstilbestrol both by the oral and by the parenteral routes of administration.

In general also there seemed to be quite a decided improvement in the vague arthropathies and hypertensions associated with the menopausal syndromes in this series of patients.

The results given here indicate that the new synthetic estrogen octofollin, when administered parenterally in oil to menopausal patients, is an effective estrogen and is nontoxic in therapeutic doses.

505 Medical Arts Building.

Summary of the Clinical Results of the Investigation of the Action of Octofollin

Patient	Age	Conditions and Symptoms for Which Treatment Was Given	Dose and Frequency	Clinical Results
G. H.	45	Natural menopause, hot flashes, sweats, palpitation	2 mg. twice a week for 3 weeks, then 2 mg. once a week for 6 weeks	Almost complete control of symptoms
E. G.	44	Postoperative menopause, hot flashes, depressed feeling, exhaustion	5 mg. twice a week for 4 weeks, then 5 mg. once a week for 8 weeks	Complete control of symptoms
C. W.	37	Early menopause, scanty irregular periods, hot flashes, nervousness, low basal metabolic rate	2 mg. twice a week for 3 weeks, then 2 mg. once a week for 5 weeks	Complete control of vasomotor disturbances
G. I.	48	Natural menopause, menses irregular, hot flashes, depression	2 mg. once a week for 8 weeks.....	Pronounced clinical improvement in symptoms
H. DeV.	38	Approaching menopause, scanty periods, precordial pain and heart consciousness	5 mg. once a week for 5 weeks, then 5 mg. every 2 weeks for 3 months	Almost complete control of symptoms
H. M.	54	Postmenopausal; no hot flashes, but pressure pain in head and neck	5 mg. once every 2 to 3 weeks.....	Complete control of subjective symptoms
P. W.	42	Dilation and curettage and x-rays to uterus for menorrhagia; following this depressed feelings and backache; no flashes	5 mg. once a week for 4 weeks, then 5 mg. once every 2 to 4 weeks	Partial relief of exhaustion and backache
E. S.	39*	Hot flashes and exhaustion following high voltage x-rays	2 mg. once a week for 7 weeks.....	Complete relief of symptoms after 4th dose and no return of symptoms until 3 months after last injection
E. S.	46*	Natural menopause, severe and frequent hot flashes, day and night	5 mg. twice a week for 3 weeks, then once a week for 4 weeks; now once every 4 to 6 weeks	Complete control of symptoms; vaginal smear returned to more normal appearance
C. M.	52	Menopause; menses scanty and irregular, severe hot flashes, sweats and choking feeling, palpitation of heart	5 mg. twice a week for 1 month, then once every 1 to 2 weeks for 4 months	Complete control of symptoms with the frequent doses and fair control with doses every 2 weeks
L. D.	47	Menses irregular and infrequent for past year; exhaustion, nervousness and few hot flashes	5 mg. a week for 1 month, then 2.5 mg. every 2 to 3 weeks	Satisfactory control of subjective symptoms and improvement in vaginal smear
R. A.	52	Two year postmenopausal, exhaustion and pressure in head	5 mg. once every 4 to 6 weeks as necessary	Almost complete control of symptoms for 4 to 6 weeks with one 5 mg. dose
M. H.	52	Hysterectomy in 1934; hot flashes and vaginal irritation since in varying degree	5 mg. every 1 to 2 weeks for 3 months, then once a month	Quite complete relief of symptoms if dose is given once a month
F. W. K.	52	Menopause; severe hot flashes since menses ceased in 1941; headache and bloating	5 mg. a week for 12 weeks, then once a month	About 50 per cent relief in subjective symptoms
N. B.	36	Hysterectomy in 1941; severe and frequent hot flashes in 1942	5 mg. a week for 1 month, then every 2 to 4 weeks	Satisfactory relief of hot flashes for 2 to 4 weeks with 5 mg.
R. B.	33	Miscarriage in 1941 followed by dilation and curettage; hot flashes and depression began in 1942	5 mg. twice a week for 8 weeks, then once a week for 2 months	Hot flashes stopped after 3-4 days after first injection; relief of depression with 20 injections
H. V. D.	40	Hot flashes, depression and irregular menses	2 mg. once a week for 2 months.....	Quite satisfactory reduction in symptoms for 6 months after treatment
M. L. M.	51*	Menopause, infrequent and scanty menses, hot flashes	5 mg. once a week for 1 month, then every 2 to 5 weeks for past 4 months	Almost 100 per cent relief of hot flashes
D. M.	50*	Menopause, hot flashes, latent syphilis, treated; chronic cholecystitis; intolerant to diethylstilbestrol	2 to 5 mg. at irregular intervals.....	Control of hot flashes with 2 to 5 mg. for varying lengths of time; 5 mg. will stop hot flashes 2 to 3 weeks
E. W.	44*	Early menopause, hot flashes, night sweats, dizzy; intolerant to diethylstilbestrol	2 mg. twice a week for 1 month, then 5 mg. a week for 6 to 8 weeks	Complete relief of symptoms, complete cornification of vaginal smear
H. L.	44	Early menopause, flushing, sweating, headaches	2 mg. twice a week for 6 weeks, then 2 mg. a week for 6 weeks	Gradual and complete in 6 weeks with cornification

OCTOFOLLIN, A NEW SYNTHETIC ESTROGEN

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Since Dodds and his associates [1] synthesized the estrogenic substance diethylstilbestrol in 1938 numerous clinical studies have demonstrated that this compound is a powerful and therapeutically effective estrogen when administered either by injection or by mouth. Many investigators have shown that it may produce some undesirable reactions. The commonest clinical objection to diethylstilbestrol has been nausea, and in various series from 10 to 60 per cent of the patients treated have complained of this possibly toxic reaction. Usually nausea can be avoided by reducing the dose,[2] by giving the medication at bedtime,[3] or by using interrupted treatment.[4] A few patients do not tolerate even small doses, and Finch [5] has suggested that nausea may be an allergic reaction. Infrequent occurrence of vomiting, headache, vertigo, abdominal distress, diarrhea or dermatoses has been reported following the administration of diethylstilbestrol. Thus the dosage, and therefore the therapeutic effectiveness, of this synthetic estrogen is limited to some extent by possible toxic gastrointestinal disturbances and occasionally by other side reactions.

Attempts have been made to produce stilbestrol modifications and to synthesize other estrogenic compounds which would not cause nausea or the other untoward symptoms sometimes occurring with diethylstilbestrol. Geschickter and Byrnes [6] demonstrated that stilbestrol monomethyl ether is an estrogen of clinical value, and Elden [7] reported that only 10 per cent of his patients received no benefit from this medication. Abarbanel,[8] however, found that when stilbestrol monomethyl ether was given in doses estrogenically equivalent to those of diethylstilbestrol the incidence of nausea was similar with the two compounds. According to Bieren and Compton,[9] dihydrostilbestrol (hexestrol) is a powerful estrogen, but its effective dose in adults was ten times that of diethylstilbestrol, and nausea occurred in over 8 per cent of their cases.

New synthetic estrogens which are not related to the natural estrogens or to the stilbenes have been reported recently. Robson and Schönberg [10] demonstrated that triphenylethylene produced complete estrous response in ovariectomized mice and found this preparation to have a prolonged effect. Later these authors reported good estrogenic effect in animals with $\alpha\alpha$-di-(p-ethoxyphenyl) β-phenyl bromoethylene.[11] Macpherson and Robertson [12] in 1939 announced that triphenyl chorethylene had estrogenic activity. They recommended that the dose of this compound for adults be 200 mg. daily. The duration of action was approximately that of diethylstilbestrol, and no nausea or other side reactions were observed.

SYNTHESIS OF OCTOFOLLIN

Blanchard [13] studied the response of rats to a new synthetic estrogen, 2-4-di(parahydroxyphenyl)-3-ethyl hexane, later named octofollin. This compound is not related to stilbestrol. He found that it produced responses in rats similar to those elicited by the natural estrogens except that it was highly active when administered by mouth. Certain natural and synthetic estrogens when given parenterally or orally in large repeated doses will produce hypoplasia of the bone marrow of dogs.[14] Stebbins and Blanchard [15] observed hypoplasia of the bone marrow of rats receiving either a natural estrogen, diethylstilbestrol, or octofollin. The incidence and degree of the hypoplasia of the bone marrow was not as great with octofollin as it was with either of the two other estrogens.

Freed, Eisin and Greenhill [16] found satisfactory therapeutic response to this new synthetic estrogen in patients receiving 1.0 to 2.5 mg. daily. Results were judged chiefly by the relief of hot flushes. They reported nausea in only 3 of a small series of cases.

In 1940 [2] and again in 1941 [4] two of us summarized our studies with diethylstilbestrol in which the subjective, objective and possible toxic responses of patients to the medication were investigated. We report here a similar study with the new synthetic estrogen octofollin.[17]

CLINICAL MATERIAL AND METHODS

During the past fourteen months we have treated over 60 persons having estrogen deficiency with octofollin. Forty-four case studies are analyzed in this report, since the attendance of the remaining patients at the clinic was irregular. Of the 44 women, 30 suffered from symptoms of spontaneous menopause, 11 from artificial menopause following operation, and 3 from primary hypogonadism. No patient was treated who did not complain of severe symptoms of vasomotor instability.

The subjective symptoms of each patient were analyzed as carefully as possible and recorded in specially prepared charts prior to and during the admin-

From the Department of Medicine, Washington University School of Medicine, and the Washington University Clinics.

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istration of octofollin. Vaginal smears were taken before medication was given and at frequent intervals during the course of therapy.

In the early part of the studies each patient was given 0.5, 1.0 or 2.0 mg. daily of the estrogenic substance by mouth for six to eight weeks; however, these doses gave little therapeutic effect. Therefore the doses were gradually increased to 5 mg. or more daily. A few

TABLE 1.—*Subjective Responses of Twenty-Six Women Receiving Continuous Treatment with Octofollin*

Response	Dose in Milligrams			
	1 Mg.	2 Mg.	4 Mg.	5 Mg.
None	14	16	2	..
Slight	4	4	7	5
Fair	..	2	..	6
Good	..	..	3	8
Excellent	..	..	..	4
Total	18	22	12	23

of the patients with severe symptoms required from 10 to 15 mg. daily to obtain relief. Continuous therapy was employed in 26 cases. Of the 26 patients receiving continuous medication, 5 received the estrogen from one to three months, eight between three and six months, five from six to nine months, and 8 for nine months or longer.

Eighteen patients were given interrupted treatment. The patients at first received 1 mg. daily for fourteen days; then the octofollin was omitted for two weeks. The next month the dose was increased to 2 mg. daily for the two week period. The patients obtained slight or no relief from these doses. The following month the dose was increased to 5 mg., then to 10 and 15 mg. in the succeeding months. Of the 18 patients given interrupted medication, 7 received this type of treatment for five months and 11 for seven months or more.

For comparison with the studies on diethylstilbestrol reported in 1941, hepatic function tests were done on 9 patients receiving large doses of octofollin. The two tests employed were bromsulphalein excretion and hippuric acid synthesis.

In 26 cases complete counts of the formed elements of the peripheral blood (excluding platelets) were performed prior to and during the administration of octofollin. Repeated urine examinations were done in all cases.

RESULTS

1. *Subjective Effects.*—Good relief of symptoms of vasomotor instability was observed in 23 of the total of 44 patients receiving either continuous or interrupted treatment. Fair relief was obtained in 10 patients, poor in 4 and no improvement in 1. Hot flushes were eliminated or diminished greatly in 15, and headaches were relieved in 11 patients in whom they had been prominent complaints. Of 26 patients, nervousness was diminished in 16 and fatigability in 14.

In table 1 are presented the subjective effects of four different levels of dosage of octofollin on the 26 patients given continuous treatment. The table shows that the majority of the patients received little or no benefit with doses of 1 to 4 mg. daily. Only 2 of 22 patients were fairly satisfactorily relieved of symptoms with 2 mg. daily. Among 12 patients receiving 4 mg. daily, symptoms were greatly diminished in 3, while in 7 only slight relief occurred, and in 2 there appeared to be no change. With 5 mg. daily, 5 patients obtained slight relief, 6 fair, 8 good and 4 excellent alleviation of symptoms. When 1 patient was given 6 mg. and another 10 mg. daily, each one obtained complete relief of symptoms of the menopause.

The subjective effects of interrupted therapy on 18 patients are presented in table 2. There was little or no effect from either 1 or 2 mg. daily, given two weeks out of four. With 5 mg. daily, 6 patients obtained good relief of symptoms, 4 fair and 8 poor, while with 10 mg. for the two week period there was excellent relief of symptoms in 4 patients, good in 7 and fair in 7. When the daily dose was increased to 15 mg., the same 4 patients obtained excellent results, 7 good and 7 fair.

From these results it would seem that from 5 to 10 mg. of octofollin daily is required in the majority of cases to relieve satisfactorily the symptoms of vasomotor instability occurring in the menopause. This conclusion is at variance with the observations of Freed, Eisin and Greenhill,[16] who found that the satisfactory daily dose of octofollin was from 1.0 to 2.5 mg. Taylor and Thompson,[18] however, had to give from 30 to 50 mg. by mouth daily to produce the same estrogenic effect as 1 mg. daily of diethylstilbestrol. Nausea, vomiting, heartburn and leg cramps were much less frequently observed than with diethylstilbestrol but were noted in some instances in their series of patients receiving octofollin.

We observed few untoward reactions. Three women receiving 10 mg. doses of octofollin over a long period complained of mild discomfort in the lower part of the abdomen. Five patients given 10 to 15 mg. daily observed an increase in the white seromucoid vaginal discharge. This occurs much more frequently with diethylstilbestrol.

Nausea did not occur in any of the 44 women we treated, even with doses as large as 10 to 20 mg. every twenty-four hours. Greenhill,[16] however, reported nausea recently in 2 of 18 patients receiving 5 mg. daily of octofollin. When the dose was reduced to 2 mg. daily he found that the incidence of nausea of 39 patients decreased to 2.6 per cent.

A number of our patients had received diethylstilbestrol two to three months prior to octofollin treatment, and many of the patients felt that diethylstilbestrol had produced greater improvement in strength and energy than did the new synthetic estrogen.

TABLE 2.—*Subjective Responses of Eighteen Women Receiving Interrupted Treatment with Octofollin*

Response	Dose in Milligrams				
	1 Mg.	2 Mg.	5 Mg.	10 Mg.	15 Mg.
None	10	8	..	..	..
Slight	8	10	8	..	..
Fair	..	..	4	7	7
Good	..	..	6	7	7
Excellent	..	..	..	4	4

2. *Objective Effects.*—We employed the vaginal smear as a simple objective means to measure estrogenic activity, although we believe that the subjective results are clinically more important than the exact degree of estrogenic response determined by any objective test. Among 18 women obtaining some relief of symptoms

18. Taylor, S. G., III, and Thompson, W. O.: Experiences with a New Synthetic Estrogen for Oral Administration, Endocrinology 30: S1042 (June) 1942.

on continuous therapy with 5 mg. daily of octofollin for six to eight weeks there was an increase in the estrous activity of the vaginal smear in 3 from an inactive type or a 1 plus to a 2 plus or more, while the cellular changes in the vaginal smears of 6 patients showed a rise of only 1 plus and in 9 there was no change. Sixteen women of the total group of 26 patients on continuous therapy showed no discernible change in their vaginal smears; however, 4 of these patients had 3 plus smears at the beginning of the experiment. Thus the administration of the estrogenic substance did not produce any significant change in the vaginal smears in approximately 50 per cent of the 26 women treated with this method, and in no instance was a complete (or 4 plus) vaginal smear response produced.

Of the 18 patients given interrupted treatment, 12 had negative (inactive) vaginal smears, 4 showed 1 plus and 2 showed 2 plus smears before octofollin was given. After five to seven months of therapy beginning with 1.0, then 2.0, 5.0, 10 and eventually reaching 15 mg. daily doses for a two week period each month, 8 women had 1 plus vaginal smears, 7 had 2 plus and 3 had 3 plus.

Since in a number of the women experiencing satisfactory alleviation of their menopausal symptoms there was little if any change in the cells in the vaginal smear after prolonged therapy, it was impossible to correlate symptomatic relief with objective results.

Several patients given 10 to 15 mg. of octofollin daily noted some tenderness of the breasts and an increase in pigmentation of the areolae. We have observed similar changes more frequently in patients receiving 1.0 mg. daily of diethylstilbestrol.

Uterine bleeding was produced in 3 of the 18 women given interrupted treatment. It usually occurred seven to ten days after the discontinuance of daily doses of 5 to 15 mg. of octofollin. It did not appear when smaller doses were employed.

STUDIES OF TOXICITY

1. *Hepatic Function Studies.*—Hepatic function was studied both by hippuric acid synthesis and by the bromsulphalein excretion of 8 women given an average of 4 to 5 mg. daily of octofollin for five months. The tests were performed in all of the cases before any treatment was given and repeated after a period of five months of therapy. In 7 cases the results of the hippuric acid synthesis tests were within normal limits both before and after treatment. The values for this test in 1 case were below the level of normal both before and after therapy. The results of the bromsulphalein excretion tests on each of the 8 patients were within normal limits both before and after treatment. There was therefore no significant change in hepatic function attributable to the administration of octofollin. We[19] have previously shown that neither diethylstilbestrol nor estradiol in the doses used in the treatment of the menopause produce any demonstrable change in the function of the liver in human beings.

2. *Blood Studies.*—During octofollin therapy no abnormality in the number of erythrocytes or leukocytes among 26 patients studied was observed, while the total grams of hemoglobin and the differential counts of the leukocytes remained within the range of normal values. The only bleeding tendency that occurred was the uterine bleeding produced in 3 women by the withdrawal of the estrogenic substance.

3. *Urine Studies.*—Repeated examinations of the urine of 38 patients showed no changes that could be attributed to the medication.

ANIMAL EXPERIMENT

For comparison with the studies made by one of us[20] on the changes in the bone marrow of dogs following the administration of estradiol or diethylstilbestrol, an experiment was done to determine the effect on the bone marrow of dogs of intramuscular injections of octofollin.

Studies were performed on 2 mature, healthy male dogs, weighing 11.5 and 14.5 Kg. As in the previous experiments, the animals were kept for a conditioning period of three weeks prior to injection of the octofollin. Red and white cell and platelet counts were done on the peripheral blood two to three times a week during the control and experimental periods.

Each dog was given a daily intramuscular injection of 5 mg. of octofollin in oil for fifty days. There occurred a slight rise in the number of leukocytes in the peripheral blood of each animal at about the eighteenth to the twenty-fifth day of treatment. We did not observe the simultaneous decrease in the number of thrombocytes which occurs with much smaller doses of estradiol or of diethylstilbestrol. The amount of octofollin injected was increased to 15 mg. daily for fourteen days, and there occurred a fall in the number of thrombocytes in the peripheral blood of the smaller dog. Each animal was then given 20 mg. daily for sixteen days. At the end of this period there was a definite reduction in the number of thrombocytes and leukocytes in the circulating blood of the smaller dog. A slight thrombocytopenia was demonstrated in the peripheral blood of the larger animal. An autopsy was done on each dog at the end of eighty days of treatment, and a mild hypoplasia of the bone marrow of the smaller animal was found. There was no significant change from normal in the bone marrow of the other animal.

Each dog received approximately 780 mg. of octofollin in sesame oil in eighty days, but pronounced changes were seen in the peripheral blood of only 1 animal. A total of 210 mg. of diethylstilbestrol dipropionate in olive oil injected during twenty-one days, or an estrogenically equivalent dose of alpha estradiol in sesame oil injected during thirteen days, has been shown to produce leukocytosis, thrombocytopenia and death in dogs.[20] Our observations would indicate that diethylstilbestrol and estradiol are, by this test, much more potent than octofollin.

SUMMARY

The majority of 44 women obtained relief of the vasomotor symptoms of hypogonadism when given octofollin by mouth in doses of 5 to 15 mg. daily. Of 26 patients given continuous treatment, 15 (58 per cent) obtained good relief of symptoms, 6 (21 per cent) fair, 4 (15 per cent) poor and 1 (4 per cent) no relief. Satisfactory alleviation of symptoms was secured in 11 of the 18 patients given interrupted therapy. They

19. MacBryde, Freedman, Loeffel and Castrodale.[3] MacBryde, Castrodale, Loeffel and Freedman.[4]

20. Castrodale, Dante; Bierbaum, Olga; Helwig, E. B., and MacBryde, C. M.: Comparative Studies of the Effect of Estradiol and Stilbestrol on the Blood, Liver and Bone Marrow, Endocrinology **29**: 363-372 (Sept.) 1941.

required larger daily doses for the two week period each month than the patients on continuous treatment. Among the 18 patients receiving 15 mg. daily for two weeks each month 11 (61 per cent) obtained good subjective response while 7 (39 per cent) obtained only a fair effect.

Nausea did not occur in any of the patients studied. Three patients (8 per cent) had discomfort in the pelvis, and several women noted tenderness of the breasts and increased pigmentation of the areolae when given 10 to 15 mg. daily. Vaginal bleeding occurred after interruption of treatment in 3 of 18 cases.

The majority of our patients required from 5 to 10 mg. daily for adequate relief of symptoms. In the series given interrupted treatment the average daily dose for the two week period was 10 to 15 mg.

Objective studies gave less definite evidence of estrogenic activity. Only 9 of 26 women (35 per cent) receiving 5 to 10 mg. daily had any change in the vaginal smears, and not one of these developed a complete estrous response. A slight to moderate change in the cellular type of the vaginal smears of each of the 18 patients on interrupted treatment was observed. Twelve of these patients had inactive vaginal smears before octofollin was given. In our experience 1 mg. daily of diethylstilbestrol produces in the average case complete response in the vaginal smear in twenty-one days. Our observations indicate that, per milligram, diethylstilbestrol is at least five to ten times as potent when given orally as octofollin.

The very low incidence of side reactions, particularly of nausea, is of clinical importance. Disadvantages of octofollin are that comparatively large doses are required and that it is more expensive per milligram than diethylstilbestrol. It is, however, less expensive per clinically effective unit than oral preparations of "natural" estrogens.

Liver function tests, blood studies and urine examinations showed no toxic effects of the new synthetic substance. Octofollin in the doses used in this experiment is apparently a safe therapeutic estrogen.

CONCLUSIONS

1. The new synthetic estrogen octofollin is effective in treatment of hypogonal symptoms in women.

2. It appears to be relatively nontoxic, since nausea did not occur in this series of 44 patients, and no other toxic manifestations were observed.

3. The effective oral dose is from 5 to 10 mg. daily when continuous treatment is used or from 10 to 15 mg. daily for interrupted treatment.

Infantile Paralysis.—The normal and usual method of travel of the virus throughout the body is reported to be by the pathways provided by the nerves. This is a neurotrophic or neuronotrophic virus. It leaves no demonstrable histologic change as it travels over or through the nerve fibers, yet its spread by way of neurons is dependent on healthy normal fibers and nerve cells. For example, it cannot progress in nerve tissue that has not fully regenerated after traumatic changes. The rate of the progression of the virus in peripheral nerves to the central nervous system has been calculated by Howe and Bodian to be at the rate of 2.4 mm. per hour in the experimental animal. Such travel occurred in both the motor and the sensory fibers.—Gudakunst, Don W.: New Developments in Infantile Paralysis, *New York State J. Med.* **43**:1514 (Aug. 15) 1943.

MENINGOCOCCIC MENINGITIS AND SEPTICEMIA

REPORT OF OUTBREAK IN FOURTH SERVICE COMMAND DURING WINTER AND SPRING OF 1942-1943

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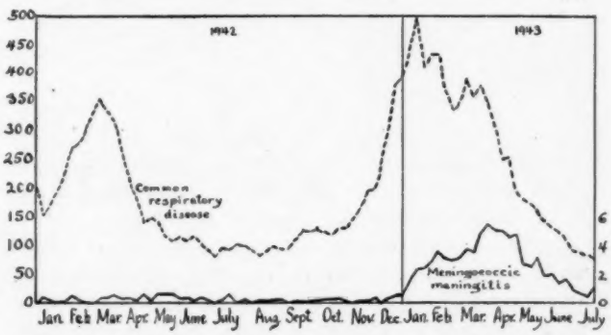
Cerebrospinal meningitis has occurred wherever large numbers of troops have been brought together. During and after World War I there were in the United States Army a little less than 6,000 cases in the course of thirty-three months.[1] The over all mortality for that series of cases was 39 per cent. Following the war the cases in the civilian population of the United States continued for ten years at a high rate, but by 1930 the incidence of cases had fallen to its usual prewar level.[2] For the years 1939, 1940 and 1941 slightly less than 2,000 civilian cases per year were reported for the whole country. The year 1942, however, showed an increase with 3,400 cases during the first eleven months.

In the Fourth Service Command sporadic cases of meningitis occurred during the years 1941 and 1942.



Relation of weekly incidence of meningococcic meningitis to that of common diseases of the upper respiratory tract as observed in 1942-1943 in the Fourth Service Command. Each figure at the left or the right represents the number of cases per thousand annually.

The case rate per thousand troops began to increase in December 1942 and what might be termed a clearcut outbreak was well on its way by the first of January. At this time simultaneous outbreaks occurred at an army station in North Carolina, at one in South Carolina and at one in Alabama, and two weeks later a camp a few miles from the first one in Alabama reported an outbreak. A large preponderance of new troops were on duty at these posts during this time.

The chief of the Medical Branch, Headquarters Fourth Service Command, has encouraged and expedited all the work mentioned in this report.

This article in brief form was read at the regional meeting of the American College of Physicians, New Orleans, April 16, 1943. The statistics have been revised to include April, May and June 1943.

Members of some fifty station hospital staffs have contributed observations and studies on cases occurring in their respective camps. A majority of the cases have come from the services of Lieut. Cols. W. B. Daniels, J. E. Knighton, O. B. Mayer, Louis Ochs Jr. and A. W. Wallace, Majors M. R. Buchman, R. W. Houseal, A. C. McCarty and A. J. Sullivan, and Capt. W. B. Malcolm. Treatment has been entirely under their control and has followed, with minor modifications, the recommendations contained in Surgeon General's Official Circular Letter No. 17 and memoranda from the Chief of the Medical Branch, Headquarters Fourth Service Command. This article does not completely express the views of the medical staff of any one station hospital but is the result of a study of their work supplemented by personal clinical and epidemiologic observation of the cases as they occurred at many of the posts.

1. Simmons, James S., and Michie, Henry C.: Cerebrospinal Meningitis, chapter IV in The Medical Department of the United States Army in the World War, U. S. Gov. Printing Office, **9**: 203, 1928.

2. Mitchell, Roscoe, L.: Epidemic Meningitis, J. Maine M. A. **34**: 45 (March) 1943.

In three of these four camps no 2 patients came from the same company or barracks, and the outbreak presented the epidemiologic appearance of being merely an increase in sporadic cases. In the fourth camp two companies had 6 and 8 cases respectively in addition to the sporadic cases elsewhere on the post. The pattern of outbreaks of meningitis is clearcut and may be stated as follows: Simultaneously at distant points an increase in sporadic cases occurred, reaching a peak in several months and declining after several more months.

In this outbreak as in previous ones the increase in case rate followed a pronounced increase in infections of the respiratory tract. This is well shown in the accompanying chart. It is to be noted that the rate of meningitis is plotted on a scale one twenty-fifth of that of diseases of the upper respiratory tract.

During World War I definite advances were made in the epidemiology of meningococcic infections. It was found that there is constantly in nonepidemic periods a carrier rate between 1 and 2 per cent. During epidemics, however, this carrier rate rises to the neighborhood of 30 per cent or higher, depending on local circumstances. Since the last war these facts have been corroborated frequently, and it has further been learned that if a high carrier rate is to be significant the organism involved must be group I meningococcus [3] since during epidemics 90 per cent or more of all cases are caused by this organism.[4]

The facts described, namely increase in sporadic cases and localized epidemics following a wave of infections of the upper respiratory tract, associated with a great increase in the meningococcus carrier rate among large groups of troops, provide evidence for a concept of the epidemiologic nature of meningococcic outbreaks. Among the new troops brought into an army post there is a rate of at least 1 to 2 per cent meningococcus carriers. If their arrival at camp occurs during the months when diseases of the upper respiratory tract are prevalent an extremely high rate of such diseases soon develops among the new troops and includes the carriers. The coughing and sneezing distribute not only the virus responsible for the diseases of the upper respiratory tract but also the meningococci introduced by the carriers. In this way the carrier rate builds up rapidly.[5] In susceptible persons during periods of fatigue and exposure the carrier state may progress into one of the clinical forms of meningococcic infection.

These facts have been carefully considered by various physicians interested in lowering the case rate of meningitis, and recommendations have been made [6] which, if possible to be carried out, would undoubtedly greatly lower the case incidence. For instance, Glover [7] in 1918 showed that avoidance of crowding by adequate spacing of cots reduced the carrier rate from 29 to 4 per cent. Others have recommended in addition avoiding exposure, fatigue and too rapid inoculation for typhoid and other diseases. However, all of these rules must be broken when it becomes necessary to build a huge army with the utmost speed. Under these conditions it is impossible to avoid all or even one of these conditions. It is fortunate, therefore, that modern methods of treatment of the patients and more recently prophylactic treatment have reached such a degree of excellence that the problem is in a fair way toward being solved by chemotherapy.

3. Branham, S. E.: The Meningococcus (Neisseria Intracellularis), Bact. Rev. **4**: 59, 1940.
4. Kuhns, D. M., Fourth Service Command Laboratory, personal communication to the author.
5. Zinsser, Hans, and Bayne-Jones, Stanhope: A Text Book of Bacteriology, New York, D. Appleton-Century Company, 1939.
6. Hitchens, A. P.: The Control of Infectious Disease in Rapidly Mobilized Troops, Ann. Int. Med. **15**: 172 (Aug.) 1941.
7. Glover, J. A.: The Cerebrospinal Fever Epidemic of 1917 at X Depot, J. Hyg. **17**: 350 (July) 1918.

STATISTICAL REVIEW

The present study comprises the cases of meningococcic infection which occurred in troops of the United States Army throughout the seven Southeastern states during the months of December 1942 and January, February, March, April, May and June 1943, the total number of cases for this period being 1,935. Table 1 shows the cases by months, and it will be seen that the incidence of cases has decreased (table 2).

TABLE 1.—*Cases of Meningococcic Infection by Four Week Periods, with Death Rate*

	Meningitis	Septicemia	Total	Mortality
December	72	14	86	12.8%
January	151	80	231	7.3%
February	216	76	292	1.7%
March	351	118	469	2.3%
April	294	158	452	2.7%
May	187	69	256	2.3%
	1,271	515	1,786	3.5%

TABLE 2.—*Cases of Meningococcic Infection by Weeks, with Deaths and Death Rate*

Week Ending		Cases		Deaths		Mortality
December	4	4		1		
	11	13		0		
	18	14		2		
	25	15		0		
January	1	40		8		
			86		11	12.8%
January	8	40		8		
	15	51		4		
	22	62		3		
	29	78		2		
			231		17	7.3%
February	5	57		2		
	12	71		0		
	19	79		2		
	26	85		1		
			292		5	1.7%
March	5	74		2		
	12	132		2		
	19	142		2		
	26	121		5		
			469		11	2.3%
April	2	133		1		
	9	124		3		
	16	120		6		
	23	75		2		
			452		12	2.7%
April	30	71		2		
May	7	81		0		
	14	50		2		
	21	54		2		
			256		6	2.3%
May	28	39		0		
June	4	46		1		
	11	36		0		
	18	22		1		
			133		2	1.5%
June	25	16		0		
			16		0	.....
Total		1,935		64		3.3%

Table 3 shows the distribution of deaths from meningitis and septicemia in new and in seasoned troops. An arbitrary period of three months' service was taken to define new from seasoned troops. It will be seen that slightly more than two thirds of the fatal cases developed among new troops (table 4). It must be remembered, however, that the final significance of this fact can be determined only when the numbers of new and old troops can be compared, and for military reasons this information is not yet available. Ordinarily

cases showing a clearcut increase in cells in the spinal fluid would be classified as cases of meningitis but the fatal cases have been divided according to the principal cause of death. If the count in the spinal fluid had not reached more than 400 cells before death the patient was classified as dying of meningococcic septicemia, although it is realized that this may be a distinction without a difference. Nearly half the deaths (23 of 51 cases coming to necropsy) occurred in cases in which meningitis had not developed to a point where the cellular response in the spinal fluid was impressive. That response is interpreted as an index of severity of infection, and this is borne out by the finding of hemorrhages in the adrenals in 16 of these cases.

At several posts Major John J. Poutas obtained information on the proportion of cases coming from urban or rural districts and found that there was no difference. This suggests that during nonepidemic periods urban dwellers are no more exposed to group I meningococcus than rural dwellers.

Mortality.—At first glance (table 1) there seems to be some discrepancy between the general mortality and the higher mortality during the months of December and January. If this is broken down into individual weeks (table 2) it will be seen that the mortality for the 40 cases during the week ended January 1 was 20 per cent. This unusual occurrence gave rise to immediate activity in the Fourth Service Command Headquarters and notices were sent out to all surgeons of the Fourth Service Command warning them about the presence of meningitis and meningococcic septicemia and advising prompt therapeutic measures. In retrospect it seems that the high mortality for that one week was caused by a combination of circumstances, since the virulence of the disease and the number of new troops have remained essentially the same. The deaths occurred largely at new posts, where the medical personnel was new to military medicine. In addition to this, sodium sulfadiazine for intravenous use was not available at most of the hospitals at that time. Some of the patients were admitted in the evening and were seen only by the officer of the day, who in many instances was a member of one of the surgical branches of the staff and therefore not thoroughly familiar with cases of meningococcic septicemia. Finally, and perhaps most important, few of the reserve officers on duty in the medical corps had had previous experience with cases of meningitis, and most of them had never seen a case of meningococcic septicemia.

Table 3.—*Distribution of Deaths from Meningitis and from Septicemia Among New and Seasoned Troops (Dec. 1, 1942 to March 26, 1943)*

	Total	New	Seasoned
Meningitis	38	23	15
Septicemia	26	21	5
Total	64	44	20

Table 4.—*Mortality from Meningococcic Infection in New and in Seasoned Troops (Dec. 1, 1942 to March 26, 1943)*

	Cases	Deaths	Mortality
New	1,219	42	3.44%
Seasoned	567	20	3.53%

Active interest was aroused in the entire subject of meningococcic infections. Local scientific meetings were held, and discussions in regard to therapeutic measures were engaged in. Improved cultural technic for isolating the meningococcus was prepared and distributed to laboratory officers at station hospitals by the Fourth Service Command Laboratory. This interest spread also throughout the unit medical officers with troops so that within ten days all medical officers of the command were on the lookout for cases, and directions prepared for the treatment of patients brought into hospitals during the night were posted by the chiefs of the medical services of the various station hospitals. At station hospitals where cases were numerous a member of the contagious disease section of the medical service was placed on night duty, so that all details of diagnosis and treatment were carried out promptly and accurately. In addition to this the nurses on night duty throughout the hospital were alerted to the possibility of patients developing signs of coma or exhibiting cutaneous rashes. Whether the additional therapeutic measures which were used and are described later as adjuncts in the section on treatment added anything to the reduction in mortality is not perfectly clear, but this remains as a distinct possibility. It seems probable that all members of the medical corps on duty in the zone of interior during the past few months will continue to be on the watch for cases of meningococcic infection and will be familiar with proper treatment, so that it is safe to prophesy that the mortality rate for the remainder of this war will be held to a low level.

The mortality figures for this series include a number of patients who died in the hospital before their condition was recognized and who received no specific therapy. In addition one patient is included who died before he was admitted to a hospital. These facts suggest that a perfect system of early diagnosis leading to prompt treatment would reduce the mortality still further. That this has already been attained to a high degree may be seen from the statement that at one post while 108 patients were being treated with a mortality of under 3 per cent there were in the county 8 civilians with the disease, 4 of whom died—a mortality of 50 per cent.

The report of meningitis throughout the state of Maine for the year 1942 gives a mortality of "something over 14 per cent, which is very low." [2] There are eight rather large posts in the Fourth Service Command where an aggregate of 161 patients with meningococcic infection were treated without a death. There were 49 other patients scattered throughout twenty-one small posts without a death. These facts are brought out to show merely that even in a single command mortality rates differ from post to post, depending on the number of cases of fulminating infection that are encountered. Eight patients with meningitis received no specific treatment, and in 8 others treatment was started so late as to be almost hopeless. With regard to the 17 remaining patients, retrospective improvements in therapeutic technic are possible. These improvements fall into all the various aspects of modern therapeutic procedures such as proper administration of sulfonamide compounds, control of fluid balance, control of electrolyte balance, control of intracranial pressure, avoidance of distention of the bladder, sedation and nourishment. Fulminating infection may require certain adjunctive measures as well. In most large hospitals one or two medical officers have become expert in these procedures and have been given complete responsibility for the entire treatment of all

patients with meningococcic infection. This specialization has produced noticeable improvement in methods and results. Any comparison of army mortality with civilian mortality requires consideration of various factors, but the excellence of army practice remains a matter for justifiable satisfaction.

CLINICAL VARIETIES OF MENINGOCOCCIC INFECTION

During the course of the years 1941 and 1942 sporadic cases of meningococcic infection were encountered in the army throughout the entire country. The infection consistently conformed to the usual pattern of cerebrospinal meningitis with a history of chilliness, frequently of chills, sore throat, headache and occasionally a gastrointestinal upset. Examination of the patients revealed fever, leukocytosis, drowsiness, stiff neck and often petechial lesions of the skin, and the spinal fluid contained between 1,000 and 20,000 cells, predominantly polymorphonuclears. Blood cultures were positive in some cases, and the spinal fluid usually contained visible intracellular or extracellular gram-negative organisms, although occasionally these were demonstrable only by culture. Spinal puncture was performed once for diagnostic purposes and occasionally a second time to prove cure or to differentiate drug fever from persistence of meningitis. In a few cases relief of excessive intracranial pressure by spinal tap quieted extreme restlessness for some hours, and in 1 case it was performed with benefit four times in the course of twenty-four hours. In another case extreme Biot breathing was relieved by several taps during the early hours of the disease and one or more patients might in retrospect have been saved by this procedure. Otherwise no useful purpose was gained by repeated spinal taps. In 2 cases death seems certainly to have been precipitated by the production of a pressure cone causing sudden unexpected death.

A Schematic Diagram of Meningococcic Infections

- Carrier state = asymptomatic
- Infections of upper respiratory tract = sore throat, otitis media or conjunctivitis
- Septicemia
  - Chronic = recurrent chills and fever
  - Subacute = arthralgia, rash; meningitis may develop
  - Acute
    - Moderate = meningitis
    - Severe = fulminating

Forms of meningococcic septicemia.

During December a few cases of meningococcic septicemia made their appearance, and the number rapidly increased during January, so that during the last two weeks in January there was a total of 61 cases. It seems fairly certain now that every clinical meningococcic infection with the possible exception of a variety of infection of the upper respiratory tract consists at some stage of an invasion of the blood stream by the causative organism. In most instances the organism localizes in the meninges, producing clinical meningitis, but in certain cases this does not eventuate. Meningococcic septicemia can be divided into acute, subacute and chronic forms, as shown in the accompanying outline.

Acute Forms.—Acute meningococcic septicemia early in its course presents a picture similar to grip or streptococcic sore throat with headache, chilliness or chills, backache and muscle ache. Soon this picture is apt to change, however, and restlessness and drowsiness supervene, often progressing rapidly to coma. Frequently the patients are brought into the hospital in a comatose state. The most fulminating type of infection ends fatally in the course of a few hours. One patient at a Southern camp was drilling at 10 a. m. when he reported feeling bad and at 1 p. m. he died. This same fulminating type of disease has been observed throughout the command in about 12 instances. In 6 of these cases organisms were seen in the peripheral blood smear.

Many of the patients with fulminating infection were admitted to the hospital in a state of shock with blood pressure between 50 and 80 mm. of mercury. Frequently such patients had evidence of widespread hemorrhages throughout the skin and mucous membranes. Usually the spinal fluid of patients with this type showed few if any cells. Many of the patients were thought to have had hemorrhages into the adrenal glands (Waterhouse-Friderichsen syndrome). Among patients with fatal infection there were 26 who died during the period of acute septicemia before meningitis developed. Autopsy was performed on 23 who died of septicemia, and hemorrhages into the adrenals were present in 17. In an additional patient edema and congestion of the adrenal glands were noted.[8] Great efforts have been made to evolve a form of treatment which would enable such patients to be cured, and this regimen includes the various adjunct measures described in the paragraph dealing with treatment. Bacteriologic correlation has not been worked out but all three groups of meningococci are represented in this small series of 14 fatal cases. It will be recalled that in children organisms other than meningococci are held to be responsible for fulminating septicemia associated with hemorrhage into the adrenal glands. The only organism other than the meningococcus which has been encountered in such cases in this group is Neisseria catarrhalis, which in 1 fatal case was the only organism recovered. Its exact significance is unknown but it was thought probable that the meningococcus had been present but was not demonstrated in the cultures.

Patients with slightly less severe septicemia lapse into coma from which they are aroused only by rapid and heroic treatment. They may show petechial or ecchymotic cutaneous lesions which in some develop into huge purpuric areas. These lesion of the skin are apt to develop rapidly, and on many occasions medical officers have noted that new lesions developed under their observation while they were performing spinal tap. An entirely different cutaneous eruption has been observed in many cases of both chronic and acute septicemia. This has been described in the British literature, and in the *Lancet* in 1941 Majors Dickson and McKinnon and Captains Magner and McGillivray[9] gave an excellent account of it as it occurred in a Canadian army general hospital. The lesions appear in groups of a few or dozens and most commonly on the limbs or trunk. They are round, well defined, maculopapular, often tender, 5 to 35 mm. in diameter, usually with dark red or purple centers. The pink area fades on pressure but the dark central spot does not. These lesions are apt to become more hemorrhagic in the

8. In 3 fatal cases of meningitis hemorrhages into the adrenal glands were discovered at necropsy.

9. Dickson, R. C.; McKinnon, N. E.; Magner, D., and McGillivray, N. B.: Meningococcal Infection, Lancet **2**: 631-634 (Nov. 22) 1941.

course of a day or two, and as the patient improves they fade in two to four days, leaving small pigmented areas. Excellent descriptions of this form of eruption have been made by several medical officers in the Fourth Service Command.[10] At posts where many such cases have been seen this rash is recognized as characteristic enough to establish the diagnosis of meningococcic septicemia. The Canadian authors emphasized the fact that localized pain or tenderness of muscles is a symptom which differentiate meningococcic septicemia from other forms of acute infection. In many of our army posts it has been noticed that acutely inflamed joints or merely exquisitely painful joints have been complained of in many instances.

Differing from the acute severe and the acute fulminating infections are others which can be called acute mild meningococcic septicemia. The onset is like that already described, but the patients do not seem to be particularly ill; they respond immediatelv to treatment with sulfonamide compounds and are well in a day or two. In fact 3 patients, each having a blood culture positive for meningococci of group I, recovered spontaneously without drug or serum therapy before the culture was known to be positive. Many similar patients with characteristic cutaneous eruptions but with negative blood cultures are believed to have a meningococcic infection falling in this mild group but have not been included in the statistical study.

Chronic Forms.—Chronic meningococcic septicemia presents a picture which frequently may be mistaken for malaria, either tertian or quartan, or some form of relapsing fever. The patient suffers from episodes of chilliness, fatigue, headache, general malaise, fever, leukocytosis and usually one or the other of the cutaneous lesions described in the foregoing paragraphs. The disease may continue on its relapsing course for several months unless the patient is treated, although spontaneous recovery occasionally occurs. The diagnosis is frequently aided by a special technic blood culture, which is most apt to yield organisms if taken while the patient is having a chill.

Subacute Forms.—Subacute meningococcic septicemia simulates rheumatoid arthritis or acute rheumatic fever and is frequently associated with fluid in the knee joints. The patients occasionally improve under nonspecific symptomatic treatment but more often they develop in a week or two signs and symptoms of meningitis, at which time the diagnosis becomes apparent. Routine cultures from the joint fluid sometimes provide the diagnosis, and in a few cases culture of the joint fluid has been positive after several days of chemotherapy. In other instances the characteristic cutaneous eruption gives rise to the correct diagnosis.

In epidemiologic circles the carrier state is considered as a subclinical, asymptomatic form of meningococcic infection. In addition to this it is thought by many that nasopharyngitis can be produced by meningococci and a number of cases of conjunctivitis (7 cases have been confirmed bacteriologically at one station hospital) and otitis media have been shown to be caused by this organism.

COMPLICATIONS

In patients receiving early chemotherapy complications are extremely rare. Statistics are not yet available, but a personal survey of this service command has left me with a recollection of a few patients with deafness (3 such patients have been discharged from the army on account of residual deafness), a few with diplopia who recovered, and a few with stiff joints, who recovered completely or partially. One patient was left with a persistent paralysis of the right serratus maximus muscle. Hematuria is seen frequently before any therapy is started but no nephritis has been seen during convalescence. Retention of urine with distention of the bladder is frequently seen in comatose patients, and in these catheterization may reduce restlessness. Accompanying encephalitis has produced coma early and a few of the patients with the fulminating form of septicemia have been brought to the hospital following the initial symptom of convulsions. Several others have died before the true nature of the condition was discovered. Bronchopneumonia occurred occasionally and was seen at necropsy. In most of the patients who recovered from meningitis cure was complete, although a few soldiers continued to complain of recurrent headache for some weeks or months and psychoneurosis has been noticed in some.

Four patients have had large sloughs involving the skin and subcutaneous area in the location of confluent purpuric areas. Two of these required skin grafting.

On the whole, complications have been conspicuous by their rarity.

POSTMORTEM OBSERVATIONS

Final reports of the postmortem examinations have not been received. Several facts stand out from the gross examinations. Usually in septicemia there were widespread petechial hemorrhages in the meninges and many other organs and often also gross hemorrhages into the adrenal glands. Hemorrhage was associated with, or secondary to, localized thrombosis of the vessels in some cases. In many of the thoroughly treated patients with meningitis clearcut evidence of the exact cause of death was lacking. One finds such statements as "In summary, the remarkable thing about this autopsy was the absence of positive findings." In cases in which there was a high cell count in the spinal fluid during life—sometimes as high as 19,000 polymorphonuclears—as well as visible and recoverable meningococci, little evidence of meningitis was apparent in the gross specimens at postmortem examination. The meningitis might be said to have been practically cured, but irreversible effects of sepsis seem to have caused death. In every fatal case several possible causes of death presented themselves. Some patients seem to have died of respiratory failure either from toxic effect on the respiratory center or from increased intracranial pressure with Biot breathing. Patients who die of septicemia die in shock, and most of them also develop acute pulmonary edema. This pulmonary edema occurs in untreated as well as treated patients and may be part of the picture of shock or it may be produced by the acute myocarditis seen in some cases. Liberal quantities of fluids injected intravenously and large doses of sulfonamide compounds, which are capable of producing myocardial and renal lesions, may be considered also as contributing causes, but I have seen no worth while evidence that can incriminate these therapeutic agents. Of 64 fatal cases 51 were examined post mortem. In 2 cases crystals were present in the renal substance although anuria had not developed. In a number of cases tubular lesions were present and many had been produced by sulfadiazine. It is also to be remembered that nephritis is a complication of

10. In the older American writings these lesions are spoken of as resembling rose spots or erythema nodosum.[11]

11. Herrick, W. W.: Text Book of Medicine by American Authors, edited by R. L. Cecil, Philadelphia, W. B. Saunders Company, 1942.

meningococcic disease. Further light on this subject is hoped for from careful clinical and pathologic study of fatal cases. Correlation of the types of organisms with the different varieties of fatal cases is being undertaken. From present information 13 fatal cases of meningitis yielded group I Neisseria intracellularis, 2 group II and 1 N. catarrhalis, while from 12 cases of septicemia there were 7 with group I, 2 with group II, 2 with group II A, and 1 with N. catarrhalis (table 5).

BACTERIOLOGY

Studies of organisms encountered in the outbreak have yielded the usual percentage for each of the various groups. The organism most often recovered is group I meningococcus. Group II meningococcus has been found in only 2 or 3 cases. Group II A was found in about one tenth of the cases. These findings are similar to those reported in other outbreaks.

In more than half of the instances in which the diagnosis of meningococcic meningitis was made there was bacteriologic confirmation in the laboratories of the various station hospitals. A large number of the patients with positive spinal fluid cultures also had positive blood cultures. The numbers of positive cultures reported are directly related to the grades of efficiency of the individual laboratory units, and in view of the wide distribution of the reported material the average level of laboratory diagnoses appears high. During an epidemic there may be more clinical diagnoses unconfirmed by bacteriologic studies than would be permissible in a period of sporadic meningitis. Several specimens of spinal fluid containing only from one to five cells have yielded meningococci on culture. In the case of one of these the fluid was tapped six hours later and then contained 4,000 pus cells.

TABLE 5.—*Thirty-Three Fatal Cases Divided According to Type of Organism*

Meningococcus Group	I	II	II A	N. Catarrhalis
Meningitis	16	1	2	0
Septicemia	8	1	4	1

TREATMENT

The amazing reduction in mortality from 39 per cent in the last war [1] to less than 3.5 per cent in the present war is due entirely to chemotherapy.[12] It is true that the most desperately ill patients may require additional therapeutic measures but for over 95 per cent of all patients chemotherapy properly administered is the only specific form of treatment necessary.

Of the various sulfonamide compounds sulfadiazine has up to the present proved to be the most satisfactory in the treatment of meningococcic infections. It is more efficacious than sulfanilamide, and with one important exception it is much less toxic than sulfapyridine and sulfathiazole. The sodium salt is available for intravenous treatment and can be administered in 5 per cent concentration in distilled water or in 1,000 cc. of isotonic solution of sodium chloride. If all patients could be given a diagnosis and treated at the onset of the first symptom, it is my firm belief that the mortality would be reduced to zero. However, the disease is often masked by the absence of pathognomonic symptoms and by the simultaneous occurrence of many infections of the upper respiratory tract presenting similar symptoms. This leads inevitably to loss of time in treatment in a few cases. In other cases the infection is so virulent that the patient dies before treatment can be given or before treatment has an opportunity to stem the tide of infection.

Treatment of carriers with sulfonamide compounds has been reported from England,[13] Australia and various small groups in the United States.[14] Fairbrother [13] found only one carrier in a group of 139 patients in a British military hospital who were undergoing treatment for another disease with sulfapyridine (total dose about 22 Gm.) while a control group contained 22 per cent carriers. He then treated 13 known carriers with 10 Gm. in three days and eliminated meningococci from the nasopharynx in all 13. Mueller,[14] during the course of a rather sharp outbreak of type I infections in New England, treated 200 persons, of whom between 60 and 70 per cent were carriers, and was unable to recover the organisms from a single one three days after cessation of the drug therapy. The dosage was 3 Gm., 2 Gm. and 2 Gm. in three days. Similar results have been obtained with even smaller doses. Prophylactic treatment has been used successfully in the United States Army in the course of the past few months. Thus one may see that small doses of sulfadiazine are capable of killing the organisms in persons designated as carriers. Patients with acute mild meningococcic septicemia can be cured by 8 to 10 Gm. in divided doses, and some have been observed to recover spontaneously. Chronic septicemia clears up on doses of 3 or 4 Gm. a day given for from five to seven days, and subacute septicemia responds to about the same dosage. Full blown meningitis responds more consistently than does acute severe septicemia. In most cases meningitis is controlled by an initial oral dose of 4 Gm. of sulfadiazine followed every four hours with 1 or 1.5 Gm. by mouth. In cases in which the infection has progressed further, with more organisms and the development of pus, somewhat larger doses may be required and more prolonged treatment may be necessary. The more severe form of meningitis may require an initial intravenous dose of sodium sulfadiazine 5 to 8 Gm. depending on the patient's weight, to be followed by further intravenous therapy if the drug does not persist at an adequate level in the blood. Finally the patients with fulminating septicemia, those who, if untreated, frequently die within two to four hours after first reporting off duty, need immediate adequate intravenous treatment supplemented by active treatment for the dehydration and shock in which they are seen. Here again 5 to 8 Gm. of sulfadiazine is given as soon as the clinical diagnosis is reached. From these remarks it is clear that the varying degrees of severity of meningococcic infection require different forms of treatment (table 5). If the infection is of the milder type the blood may be cultured and the spinal fluid examined before treatment is begun, but, if the infection is overwhelming, not a single minute should be lost in starting treatment. In large station hospitals, where most of the patients with fulminant infection have been treated, slight variations in the routine have been elaborated. There is uniform agreement as to the need for immediate intravenous treatment and equally uniform agreement as to the need for restoring body fluids as rapidly as possible. Lieut. Col. Worth B. Daniels finds that

12. Schwentker, F. F.; Gelman Sidney, and Long, P. H.: The Treatment of Meningococcic Meningitis with Sulfanilamide, J. A. M. A. **108**: 1407 (April 24) 1937.

13. Fairbrother, R. W.: Cerebrospinal Meningitis: The Use of Sulfonamide Derivatives in Prophylaxis, Brit. M. J. **2**: 859 (Dec. 21) 1940.

14. Mueller, J. H.: The Relation of the Carrier to Epidemic Meningitis, to be published.

giving the sodium sulfadiazine in 1,000 cc. of isotonic solution of sodium chloride starts both chemotherapy and restoration of fluids at the same time. At the station hospital where he is chief of the medical service best results were thought to be obtained by a somewhat smaller initial intravenous dose (3 Gm. or 3.5 Gm.). In most cases this is followed by 1,000 cc. of 5 per cent dextrose solution, and fluid is given thereafter in amounts adequate to insure abundant urinary output.

Complications.—The one disturbing complication encountered in treatment with sulfadiazine is hematuria, which is often associated with retention of nitrogen and only rarely with oliguria and anuria. It is caused by crystallization of the superconcentrated form of the drug in the tubules of the kidneys. It has been known for some time that this crystallization will not take place in alkaline solutions and that crystallization depends on a combination of concentration and acidity of the solution. That this holds true for human urine was shown graphically by Fox, Jensen and Mudge.[15] Two patients treated at the Presbyterian Hospital, New York, were given enough of the drug intravenously to produce blood levels of 69.5 mg. and 138 mg. per hundred cubic centimeters respectively. Extremely large doses of alkali, 10 to 20 Gm. of sodium bicarbonate daily, were given to keep the urine at p_H 7.5, and fluids were forced diligently. As soon as the p_H fell slightly the crystals appeared in the urine. In cases of meningococcic infection one is not dealing with such extremely high blood levels, but it is thought by most clinicians who have treated these patients for fulminating disease that it is essential to obtain promptly levels between 15 mg. and 20 mg. per hundred cubic centimeters. It must be pointed out, however, that these particular patients when first seen are dehydrated and in a condition of shock which tends to lessen renal blood flow. If the body is conserving fluids the urine will be extremely concentrated so that the percentage of drug in the tubular fluid may reach disproportionately high levels. This concentrated urine has a tendency also to be strongly acid, and forcing fluids must be undertaken at the very earliest moment. It has been the experience throughout the entire southeastern section that a large percentage of patients given intravenous medication develop hematuria, often gross hematuria, soon after the first intravenous injection. Retention of nitrogen may or may not accompany hematuria and occasionally develops even in the absence of hematuria.[16] It should be emphasized, however, that when an adequate urinary output has been established and a change made at the same time from sulfadiazine to sulfanilamide treatment, with the use of alkali, the hematuria promptly clears up and retention of nitrogen disappears. In no case has there been evidence of more than temporary functional renal impairment, and I have seen nothing in the literature to suggest permanent renal damage from sulfadiazine.[17] At one post this problem seems to have been solved successfully.[18] Desperately ill patients are treated intravenously immediately with 1,000 cc. of a sixth-molar solution of sodium lactate, followed by 5 Gm. of sodium sulfadiazine in 5 per cent concentration in distilled water, followed by 1,000 cc. of a sixth-molar solution of sodium lactate, followed more slowly by 1,000 cc. of a 5 per cent dextrose solution in 0.9 per cent saline solution. No patient treated by this technic has developed hematuria; in every one the urine was alkaline, diuresis was abundant and the blood level the following morning was usually in the region of 12 to 14 mg. per hundred cubic centimeters. There is every reason to believe that this or some modification of this technic will eliminate hematuria from crystallization of a sulfonamide compound and at the same time afford a prompt high blood level of the drug.

At certain stations the subcutaneous injection of sulfadiazine in 0.5 per cent concentration in isotonic solution of sodium chloride has been advocated, and this injection is often given soon after the first intravenous injection. It is thought that such a procedure effects a slower rate of absorption and possibly a steadier blood level. At other stations excellent results have been obtained by using a Levine tube. Through this tube fluids, nourishment and salt as well as medication can be administered. In some of the more desperately ill patients adequate blood levels have not been obtained by oral use of the drug even when extremely large doses were given. For this reason when the ordinary dosage of 1 to 1.5 Gm. every four hours does not maintain an adequate blood level intravenous medication with doses of 2 Gm. should be employed as an extra. Usually after one or two doses have been given intravenously the patient regains consciousness to a degree which permits subsequent doses to be given by mouth.

Additional therapeutic measures have been used and should be mentioned. In cases of shock due to toxemia, blood transfusion and plasma infusion have been used with apparent benefit. Also in cases of shock adrenal cortex extract has been used in doses of 30 cc. to 50 cc. followed by smaller doses at frequent intervals with much benefit in the eyes of six observers. Other observers have not been able to convince themselves of beneficial effects. Epinephrine administered by the constant drip method seems to have had brilliant results in a few cases. Desoxycorticosterone acetate has been used but with a more delayed action and without clear-cut evidence of benefit. It seems possible that in patients whose adrenal glands have been damaged by hemorrhage, but who have been cured of the bacterial infection, this synthetic drug might play a beneficial role after the early stages. Three such patients are thought to have been cured in the series now being reported, and possibly many others.

Blood Level of the Drug.—Exact information is not at hand as to what blood level of the sulfonamide compound is adequate in the treatment of each of the various clinical forms of meningococcic infection outlined in this article. In the literature are reports of cures from a dose as low as 1 Gm.[19] At the opposite end of the scale is the widespread experience that in desperately ill patients large doses by mouth fail to give levels over 2 or 3 mg. per hundred cubic centimeters. In the middle of the scale is a large group of patients who have recovered from clearcut meningitis on ordinary oral doses, whose blood level either reached 10 to 12 mg. or stayed down between 3 and 5 mg. per hundred cubic centimeters. Attention should be drawn to an article

15. Fox, C. L.; Jenson, O. J., and Mudge, G. H.: The Prevention of Renal Obstruction During Sulfadiazine Therapy, J. A. M. A. **121**: 1147 (April 3) 1943.

16. Houseal, Major R. W.: Personal communication to the author.

17. Harries (G. E.: Cerebrospinal Fever: A Review of 500 Cases Treated by Chemotherapy Without Intrathecal Serum, Brit. M. J. **2**: 423-425 [Oct. 10] 1942) has reported that a patient treated in the Cardiff City Isolation Hospital died from anuria.

18. Peters, Lieut. M. A.: Personal communication to the author.

19. Quoted by Dingle, J. H., and Finland, Maxwell: Diagnosis, Treatment and Prevention of Meningococcic Meningitis, War Med. **2**: 1-58 (Jan.) 1942.

by Dowling, Hartman, Feldman and Jenkins[20] comparing the mortality rates from lobar pneumonia in two series, one treated with an initial dose of 5 Gm. by mouth and 1 Gm. every four hours, and the other series with just half this dose. It was shown that the mortality rates were identical. It seems likely then that in many instances of meningitis excessive doses have been given and an excessive blood level has been maintained. On the other hand it seems clear that the more severely infected patients require higher blood levels than the patients whose disease is mild and moderate. This was shown to hold true for laboratory animals (mice) by Long, Bliss and Feinstone,[21] who stated that "It is to be noted that the larger the dose of the drug the greater was the survival rate of the mice and that the average duration of life was longer for the more heavily treated mice." Patients have been observed who after two or three days on ordinary dosage have shown noticeable improvement when the size of the dose was increased. No harm has been seen from blood levels of between 15 and 25 mg. per hundred cubic centimeters, and hematuria can be avoided by forcing fluids and alkalis. The problem arises as to whether or not administration of excessive amounts of fluid washes large amounts of the drug out of the system, thereby reducing the effectiveness of the treatment. It is thought that in most infectious diseases the urinary output should be maintained at between 1,500 and 2,000 cc. in twenty-four hours, and this has proved satisfactory in cases of meningitis. The intravenous injection of fluid in the form of isotonic solution of sodium chloride and 5 per cent dextrose and sodium lactate and the administration of fluids by mouth or Levine tube should be regulated to the needs of the individual patient. Until further evidence is at hand the best rule is to obtain promptly a blood level of 12 to 15 mg. per hundred cubic centimeters and maintain a level of 10 to 12 mg. per hundred cubic centimeters until the patient is out of danger. After the first few days levels of 7 to 10 mg. per hundred cubic centimeters or even lower will suffice to complete the cure. It is my impression that the level of the drug in the spinal fluid has little practical significance since the systemic, cerebral and meningeal locations of the infection are supplied with the drug by the blood stream and those organisms which reach the spinal fluid are essentially harmless.

Antimeningococcus Serum and Antitoxin.—The problem of serum therapy has been largely discussed. My colleagues and I have nothing to add except that it is the universal opinion throughout the Fourth Service Command that ordinary antimeningococcus serum has been of no additional value in treatment. There is one group of patients who seem to have been benefited by meningococcus antitoxin, namely the group with septicemia. Some of these are so toxic that they die in a few hours. It is clear that antibacterial treatment must have time to become effective and this time can be lengthened, it is thought, by the use of antitoxin. This whole subject is in the course of being evaluated, and at the present time the supply of meningococcus antitoxin is extremely limited. The antitoxic property is contained also in concentrated rabbit antimeningococcus serum, but here again the supply of this product is extremely limited. Answers from a recent questionnaire throughout the army hospitals of the southeastern area reveal that 10 of 17 medical officers who have used antitoxin in more than one case believe it has had a distnict beneficial effect, noticeable within a few hours. One hundred and thirty-six of the desperately ill patients were given antitoxin, and at ten station hospitals the effect was thought to be either beneficial or extraordinarily beneficial in 56 cases. In 3 cases an immediate beneficial effect was noted. Those who are not impressed by its value point out that similar improvement is noticed in a few cases within two or three hours after the injection of sodium sulfadiazine. Final proof of the benefit of antitoxin therapy is not at hand. A warning must be issued that every precaution in the use of serum must be scrupulously observed, and patients with a history of allergy or recent serum treatment or those showing a positive cutaneous test should not be treated with serum or treated only after careful desensitization has been effected. There is no reason to believe that serum therapy properly administered is more dangerous to a patient in shock than to any other patient. Nor is there any reason to believe that intravenous injection of serum places any more strain on the heart and the peripheral vessels than intravenous injection of any other fluids. As long as anaphylaxis is avoided and fluids are injected into the vein slowly, no particular fear of this form of treatment need be entertained.

It is interesting to observe a graphic example of what early diagnosis and prompt efficient treatment can effect. During the first two months of this outbreak many unusual cases of meningococcic infection escaped early recognition by unit medical officers, various officers of the day and members of various sections of the hospital staffs until the disease was fairly far advanced. This with other factors is reflected in the mortality rates of 12.8 per cent for the month of December and 7.3 per cent for the month of January. During these two months only 317 patients with meningococcic infection were seen. In the next two months, after the technic of early diagnosis and treatment was learned, 761 patients were treated with a mortality of only 2.1 per cent. This excellent result was obtained by close cooperation among all the members of the army medical corps and by the individual personal attention of one or more officers who have been in charge of the patients at each of the various station hospitals. Cases of fulminating infection are still occurring, however, and are the ones which form the basis for the present mortality rate. In the month of April (which includes five weeks) there were 15 deaths out of 531 cases, so that although the outbreak is definitely receding in some areas it is continuing with full virulence in others.

COMMENT

The experience with a large number of cases of meningococcic infection during the past two months has provided opportunity for wide employment of modern chemotherapy. The mortality rate in the first two months was reduced to one fourth of the rate in the last war, and, as experience and proficiency in diagnosis and treatment were gained, this low rate was cut to one fourth, or 2.1 per cent, in 761 cases occurring in the Army throughout the seven Southeastern states during the months of February and March. The feasibility and effectiveness of large scale prophylactic use of sulfadiazine in the reduction of carriers and the prevention of cases are being demonstrated. It has been possible then to compensate by improved methods of

20. Dowling, H. F.; Hartman, C. R.; Feldman, H. A., and Jenkins, F. A.: The Comparative Value of High and Low Doses of Sulfadiazine in the Treatment of Pneumococcic Pneumonia, Am. J. M. Sc. **205**: 197-203 (Feb.) 1943.

21. Long, Perrin H.; Bliss, Eleanor A., and Feinstone, W. Harry: Mode of Action, Clinical Use and Toxic Manifestations of Sulfanilamide, J. A. M. A. **112**: 115-121 (Jan. 14) 1939.

treatment and prophylaxis for the rapid training program which necessitated fatigue, exposure and crowding of unseasoned troops. It seems safe to prophesy that in succeeding years the case rate can be greatly reduced by prompt prophylactic treatment at suitable points, particularly among unseasoned troops. It seems equally safe to prophesy that the mortality from the cases that do develop will be held to low levels, although the occasional cases of fulminating disease probably will continue to produce a small number of deaths.

SUMMARY AND CONCLUSIONS

In a series of 1,518 cases of meningococcic meningitis and septicemia, the early mortality rate of 8.8 per cent in 317 cases was lowered during February and March to 2.1 per cent in 761 cases.

Two thirds of the cases developed among new troops.

Of 55 fatal cases 80 per cent developed among new unseasoned troops.

Of 46 cases coming to autopsy 18 showed hemorrhage into the adrenal glands. This is regarded as an index to the severity of the septicemia and presents an additional feature for therapeutic consideration.

Early diagnosis and prompt skilful treatment based primarily on administration of suitable sulfonamide compounds will still be important even if prophylactic chemotherapy proves highly effective.

THE TREATMENT OF BURNS OF THE EXTREMITIES

WITH CLOSE FITTING PLASTER OF PARIS CASTS

STANLEY M. LEVENSON, M.D.
AND
CHARLES C. LUND, M.D.
BOSTON

Plaster casts have been used occasionally for many years by many surgeons for special indications in the care of surface burns. They have had particular use as splints to prevent deformity. For the most part such casts have been used in the secondary treatment of burns and have been well padded and loose fitting. Frequently they have been bivalved early to provide for frequent changes of whatever dressings were used under them. Lohr [1] in 1934 advocated the use of plaster casts over applications of cod liver oil ointment in the treatment of early burns. He attributed his good results chiefly to the cod liver oil. Roulston [2] in 1941 applied casts to burned extremities after maximum swelling had already occurred and infection was present. It was his opinion that epithelization and return of function were more rapid in these cases than in similar cases treated by other methods. Stonham [3] in India treated old burns in closed plaster and gave the opinion that there was more maceration and persistence of infection than when the wounds were left open. Zeno [4] between 1937 and 1939 published a number of articles in several countries on the use of plaster casts in fresh burns. In the two of these articles studied [5] the articles and one illustration indicate that tightly fitting casts were not used. Joints above and below the burn were immobilized but the cast was not closed over the end of the extremity. Casts were used for body burns as well as for burns of the extremities. Zeno felt that the good results obtained resulted from the immobilization provided by the casts. Afonso [6] uses fairly close fitting casts over a thin tannic acid eschar. He presents abstract case reports on 8 cases with good results. Trueta [7] recommends a close fitting cast for burns of the extremities, back and neck. He applies them over a thin tannic acid eschar after débridement. Most of his experience was with cases in which maximum swelling had occurred before the cast was applied. Cohen [8] also treated a few similar cases with casts but without tannic acid. Barnes [9] has recently reported the use of close fitting casts for burns of the hands, using a technic identical in principle to that reported here. It differs only in the use of débridement, in the use of less gauze to absorb secretions and in the insistence on suspension.

The possibility that plaster casts might serve a useful function besides providing rest and protection in the treatment of burns was not appreciated until the physiologic studies of Glenn, Peterson and Drinker [10] and of Glenn, Gilbert and Drinker [11] indicated the harm produced by the swelling of the burned tissues. They also showed that the application of a close fitting plaster cast immediately after the burn would prevent swelling and at the same time the circulation in the burned extremity was unimpaired, whereas the circulation in the untreated foot showed definite indications of impaired capillary flow. Barnes and Trueta [12] had already shown that swelling could be prevented in this way.

In their experiments Glenn and his co-workers [11] pointed out certain specifications that must be followed if the closed plaster cast treatment is to be fully successful. First, the burn must be so located that the plaster may extend a few inches above the upper edge of the burn. Second, the plaster must be closed at the lower end and fit evenly and closely to the skin at all points. Third, compression of the tissues at

From the Burn Assignment of the Surgical Services of the Boston City Hospital and the Department of Surgery of the Harvard Medical School.

The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Harvard University.

Drs. Glenn and Drinker and Mrs. Gilbert of the Harvard School of Public Health allowed us to see many of their animal experiments, made their manuscript available to us in advance of publication, showed interest and gave us advice in the treatment of our clinical cases.

1. Lohr, W.: Ueber die Lebertransalbenbehandlung (mit und ohne Gipsverband) bei frischen Verletzungen, Verbrennungen und phlegmonosen Entzündungen, Zentralbl. f. Chir. **61**: 1686-1695, 1934.

2. Roulston, T. J.: Closed Plaster Treatment of Burns of the Extremities, Brit. M. J. **2**: 611 (Nov. 1) 1941.

3. Stonham, Franklyn: Closed Plaster Treatment of Burns of Limbs, Brit. M. J. **1**: 737 (June 13) 1942.

4. Zeno, L.: Tratamiento de las quemaduras simples y complicadas mediante el enyesamiento, Bol. y trab. de la soc. de cir. de Buenos Aires **22**: 712-722 (Sept.) 1938. Zeno, L., and Berenboym, S.: Plaster of Paris Bandage in Therapy of Burns of Extremities, Novy. Khir. Arkh. **38**: 485, 1937. Zeno, L., and Kaplan, A. V.: Plaster of Paris Bandage in Therapy of Burns of Extremities, Vestnik. Khir. **51**: 16-18, 1937. Zeno.[5]

5. Zeno, L.: Tratamiento de las quemaduras simples y complicadas mediante el enyesamiento, Arch. Urug. de med., cir., y espec. **14**: 322-324, 1939; Tratamento biologico das queimaduras, Arq. brasil de cir. e ortop. **6**: 295-301, 1938.

6. Afonso, J.: Tecnica de Zeno para o tratamento das queimaduras, Arq. brasil de cir. e ortop. **6**: 302-309, 1938.

7. Trueta, J.: The Principles and Practices of War Surgery, St. Louis, C. V. Mosby Company, 1943, pp. 405-413.

8. Cohen, Solly M.: The Treatment of War Burns, Brit. M. J. **2**: 251 (Aug. 24) 1940.

9. Barnes, J. M.: Treatment of Burns, Brit. M. J. **1**: 408-410 (April 3) 1943.

10. Glenn, W. W. L.; Peterson, D. K., and Drinker, C. K.: The Flow of Lymph from Burned Tissue, with Particular Reference to the Effects of Fibrin Formation on Lymph Drainage and Composition, Surgery **12**: 685 (Nov.) 1942.

11. Glenn, W. W. L.; Gilbert, H. H., and Drinker, C. K.: The Treatment of Burns by the Closed Plaster Method, with Certain Physiological Considerations Implicit in the Success of this Technic, J. Clin. Investigation **22**: 609 (July) 1943.

12. Barnes, J. M., and Trueta, J.: Absorption of Bacteria, Toxins and Snake Venoms from the Tissues: Importance of Lymphatic Circulation, Lancet **1**: 623 (May 17) 1941.

the time of application must be avoided. Fourth, the benefits of the treatment decrease according to the amount of swelling that precedes the application of the plaster. Their demonstration of the safety, comfort and good end results secured by this method were so impressive that application of the method to human burns has been made, although it is seldom possible to treat the latter before some swelling has occurred.

METHOD

If shock or other systemic disturbance is present, it is treated by accepted practices at the time the cast is applied. There is but little shock caused by the treatment itself, as no anesthesia, débridement nor cleaning is done except for the removal of large pieces of loose, hanging skin. This preliminary procedure is recommended for human burns by Cope [13] and has been demonstrated by him to give good results when combined with the pressure dressings of Allen and Koch.[14]

One layer of sterilized petrolatum gauze is applied to the skin over the whole area to be covered by plaster. This is fitted exactly and is carefully placed between the fingers. This petrolatum gauze is cut from 44 mesh 3 inch wide rolls of bandage. This layer is covered with four layers of sterile open mesh gauze, fitted carefully without overlapping. The gauze does not go between the fingers but does surround the thumb. Boston City Hospital abdominal sponges happen to be

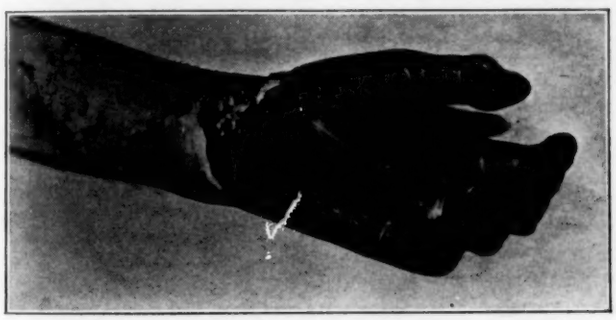


Fig. 1 (case 1).—Appearance of hand before treatment. Note broken and unbroken blisters. Sooty appearance from electric flash.

folded in such a way, 24 inches long and 4 inches wide, that they are convenient for this purpose. Very thin plaster slabs are then moistened and molded over the extremity front and back. A thin layer of rolled plaster completes a nearly skin tight, light, well fitting plaster which extends 3 to 4 inches above the burn. The fingers are placed in a semiflexed position. Fifteen hundred units of tetanus antitoxin is given at once and this dose is repeated in five days. Sulfadiazine is started in twelve to twenty-four hours only in the cases in which, in addition, severe burns are present in other parts of the body. It is continued as long as it seems to be indicated. The original cast is left in place for fourteen days. If the burn has not healed at the time of its removal, another is applied at once and left on for a further period of fourteen days, since infection, if present, sets in motion a train of events (increased lymph flow, swelling and so on) fundamentally similar to that following the original thermal injury. Further treatment, if necessary, after the fourth week is by other methods. Surface cultures are taken on admission and at each subsequent dressing.

13. Cope, Oliver: Care of the Victims of the Cocoanut Grove Fire at the Massachusetts General Hospital, New England J. Med. **229**: 138 (July 22) 1943.
14. Allen, H. S., and Koch, S. L.: Treatment of Patients with Severe Burns, Surg., Gynec. & Obst. **74**: 914-924 (May) 1942.

REPORT OF CASES

All the burns studied in this series were of the hands and arms. It is our intention to treat burns of the feet and legs in the same way, but no suitable cases have been available to date. The cases are numbered in order of admission to the hospital. They are divided

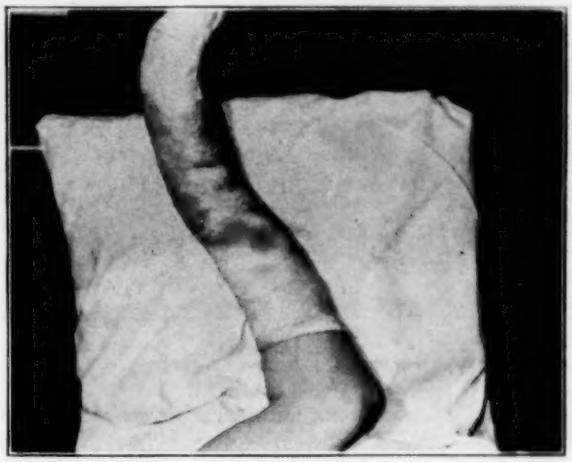


Fig. 2 (case 1).—After five days. Note median position of fingers. Slight exudate stains the cast.

into two groups. Group 1 is made up of those with burns that proved not to have total destruction of skin in any areas of the hands or arms (second degree burns) and group 2 of cases with burns of the hands that have proved to have destruction of full thickness of the skin in one or more areas (third degree burns).

GROUP 1

CASE 1 (Figs. 1-5).—An electrical worker aged 33 swung a lantern against a "third rail." The electric flash knocked him down. Examination showed the left hand covered on both sides with soot, slight swelling and a few intact and many ruptured blebs of skin. The surface area involved was about 2 per cent. Cultures were taken from the surface and petrolatum gauze strips and a cast applied ninety minutes after the time of injury. During the first forty-eight hours there

Fig. 3 (case 1).—After twenty-four days. Second cast removed. Note ability to flex hand.

was a dull pain in the hand and wrist but no throbbing or paresthesia. At twenty-four hours there were slight edema and redness proximal to the cast for 2 inches on the mesial side. Because of the swelling he was given oral sulfadiazine for one week, starting at thirty-six hours. The swelling subsided in two days. There was no lymphadenitis or lymphangitis. He was afebrile throughout. A small area of staining from exudate appeared on the cast. The culture from the burn

surface was reported to show alpha hemolytic streptococcus, hemolytic Staphylococcus aureus and Bacillus subtilis.

At eleven days the cast was removed. This was a painless procedure. There were small amounts of moist exudate present, particularly on the anterior wrist. The layer of soot and dirty epithelium was intact on the hand. Because of the deeper burn at the wrist which had not completely healed, a new

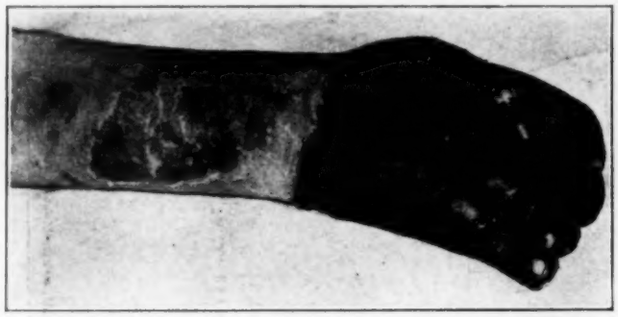


Fig. 4 (case 1).—After twenty-four days. Second cast removed. Note hand in median position.

cast was applied. Culture at the wrist showed alpha hemolytic streptococcus, hemolytic Staphylococcus aureus, Clostridium perfringens and Pseudomonas aeruginosa, with the latter predominating.

During the next two weeks absence of fever and pain continued and there was no swelling proximal to the cast. At twenty-four days from injury the second cast was removed. The wrist burn was partly healed.

The burns of the hand had completely healed under the dark layer of desquamating epithelium. Motion of the fingers was fairly good. There was no pain. A small petrolatum dressing was applied to the wrist. At five weeks all desquamating epithelium was off the hand, the wrist was healed and motion in the hand and fingers was normal.

Case 4 (Figs. 6 and 7).—An electrician aged 34 was burned in an explosion of an oil heater. He had burns with blisters and broken blisters of both sides of all fingers, both hands and both wrists and of the right forearm, elbow, part of the arm and part of the face. About 10 per cent of the surface area was involved. There was also some respiratory irritation from inhalation. Surface cultures were not taken on admission. Casts were applied over petrolatum gauze dressings ninety minutes after the accident. The patient was moderately dyspneic

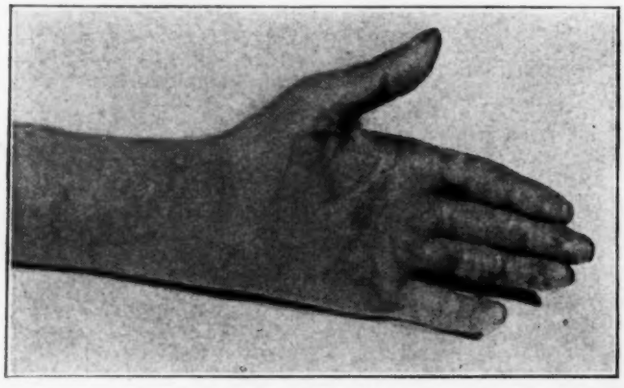


Fig. 5 (case 1).—After forty days. Complete healing with excellent function was present for ten days before this picture was taken.

and there were crepitant rales throughout the lung fields. The temperature rose to 102.0 F. the first two days, fell to 100 on the fourth day and remained normal thereafter. Oral sulfadiazine was started at twelve hours. It is our impression that this fever was of pulmonary origin. The casts were removed on the eleventh day and second casts were applied. There was no swelling or sepsis, and minimal exudate was present. Motion was good. Cultures at this time showed alpha hemolytic streptococcus, hemolytic Staphylococcus aureus, Bacillus subtilis and Pseudomonas aeruginosa present on both hands. At twenty-three days, when the second casts were removed, healing was complete and function was good.

Case 5.—A member of the fire department aged 43 had to escape from a roof through a wall of flame. He received a first degree burn of his face, small second degree burns of both knees and second degree burns of both hands. The surface area involved was about 5 per cent. Many broken blebs were present. The dorsum of the right hand and fingers was covered with large unruptured blebs. Without cleaning, petrolatum gauze and casts were applied to both hands and forearms two hours after the injury. His hands were very comfortable in the casts and there was no fever. At two weeks the casts were removed. The left hand was healed and normal. The right hand was covered with a thick layer of desquamating epithelium. Motion of wrist was normal and of fingers 60 per cent. A cast was applied to this hand for two weeks more. At four weeks healing was complete and motion of fingers was very good.

Case 6.—A member of the fire department aged 30 was burned at the same time and in the same way as patient 5. His burns were less severe. There were burns with blisters of the dorsal aspect of all fingers and of both hands and additional burns of the face. The total area was about 3 per cent. Casts were applied to both hands up to the midforearm.

Fig. 6 (case 5).—Eleventh day. Condition on removal of first casts. Note free flexion.

Cultures on admission showed "no growth." Normal recovery occurred. On removal of the casts at fourteen days complete healing had occurred. Motion was normal. There was no exudate on the dressing.

Case 7.—A schoolboy aged 9 years lighted a pile of gunpowder and received burns of the right hand and face. There were blisters on the right hand and fingers and a large denuded blister of the right wrist. A moderate amount of soot was present in the burned skin. The total area was 4 per cent. Cleaning was not done. Petrolatum gauze and a plaster cast were applied two hours after the accident. Culture showed "no growth." The temperature went daily to 100 F. for one week, with no rise thereafter. The cast was removed on the fourteenth day, when healing was complete and function normal.

Case 8.—A man aged 63 received gasoline flame burns of the second and third degree of the entire right leg and thigh, the inner aspect of the left leg and thigh, the lower part of both buttocks, and a long narrow strip across the abdomen. Parts of these burns were dirty dead white, parts were leathery and still other parts were oozing from broken blisters. The right hand also was burned and showed blebs and broken blebs over the dorsum of all fingers, the hand and wrist. The total area of the body burned was 25 per cent. A cast was applied to the hand and forearm, but other treatments to the legs and abdomen. He was given 1,500 cc. of plasma in the first twenty-four hours.

The hand was very comfortable in the cast. On the fourth day he developed bronchopneumonia, although on sulfadiazine

treatment from the twelfth hour. After a week he began to improve but remained a very sick man. On removal of the casts at fourteen days the hand was completely healed and motion was normal.

CASES WITH DEEP BURNS OF THE HAND

CASE 2.—A chronic alcoholic addict aged 32 set his bed on fire smoking. He was moderately intoxicated and had a blood plasma alcohol level of 0.026 Gm. per hundred cubic centimeters. There was a deep burn of the whole circumference of the right arm from the finger tips to the axilla. It extended over the shoulder and down the flank to the lateral abdominal wall. This whole area was burned so that the skin was leathery and not weeping. There was a less severe burn of the left hand from the finger tips to the upper forearm. The total area was 20 per cent. Both hands and arms were placed in plaster casts. On the right arm a petrolatum dressing compressed with an Ace bandage was continued above the cast to cover the remainder of the burn on the shoulder and axilla and over the flank.

During the first twenty-four hours he was given 4,000 cc. of plasma and in the second 1,000 cc. His blood pressure was always maintained, but his urine output was only 300 cc. the first twenty-four hours. He went into very severe delirium tremens that did not respond well to very large doses of vitamins or to the usual doses of paraldehyde. On the fourth day he had some symptoms of pneumonia, but adequate chest

Fig. 7 (case 5).—Twenty-third day. Condition after removal of second casts and cleaning. Complete healing and complete return of function.

examination could not be made because of large body dressings. On the eighth day spastic symptoms suggested meningitis, but a lumbar puncture secured normal spinal fluid. This stiffness did not suggest tetanus and improved steadily up to the time of his death. Death occurred on the ninth day.

The casts were removed post mortem. Complete destruction of the skin over nearly all the burned area was seen. This destruction was as severe where no cast was applied as it was under the cast. There was much more moisture and other evidence of infection in the areas not treated with the cast than under it. However, the skin of the third, fourth and fifth fingers of the right hand was almost completely destroyed, so that the posterior tendons were exposed as well as the proximal interphalangeal joints. In spite of this destruction there was obvious circulation still maintained to the tips of these fingers on the palmar surface. The autopsy showed that death had occurred as a result of massive bronchopneumonia.

CASE 3 (Figs. 8, 9 and 10).—A housewife aged 35 was removed, deeply intoxicated and burned, from a burning apartment. A strong odor of alcohol was present and the blood plasma alcohol level was 0.056 Gm. per hundred cubic centimeters. Crepitant rales were present in both lung fields. There was definite exposure to smoke inhalation. There were burns of the whole hand and forearm to 1 inch above the elbow. Over this area most of the blisters had broken and the epidermis was missing. Much of the skin was leathery and dry, especially the last three fingers and a large area below the elbow. These areas appeared to be third degree burns. There was also a burn of the lateral surface on the left leg and buttock that was dry, brown and leathery in appearance. There were other severe burns of the right buttock and slight burns of the face. The surface area involved was 15 per cent. A cast

Fig. 8 (case 3).—Thirteenth day. Cast and dry gauze removed. Petrolatum strips in place. Note small amount of exudate.

was applied to the arm up to the axilla with the elbow extended to 120 degrees. Other dressings were applied to other areas. During the next few days the patient was very sick with delirium tremens and pulmonary irritation.

At thirteen days the cast was removed. It was remarkable in two ways: First, there was but little pain in removing it and secondly there was very little discharge on the dressing. There was dry leathery natural eschar of the skin of the medial three fingers. Another cast was applied and left on ten days. When removed, it was seen that the extensor tendons of the medial three fingers were exposed over the proximal interphalangeal joints. There was but little pain and tenderness and little swelling. Motion was good even in these fingers. Following removal of the second cast, treatment was shifted to irrigation in a "Bunyan" envelop. She was ready for grafting on the fifty-second day, but the presence of scarlet fever in the ward caused a delay. On the sixty-sixth day Padgett dermatome grafts were applied to all areas of granulation on the hand, forearm and leg. On the seventy-sixth day at the first dressing of the grafts, all had taken except over the exposed bones of the three lateral fingers.

Fig. 9 (case 3).—Thirteenth day. Petrolatum strips removed. Note minimal swelling.

COMMENT

A satisfactory treatment for burns should be locally and generally harmless, comfortable and easy to apply from widely available materials of minimum bulk. It should also give protection against the invasion of harmful organisms and protect the natural defenses of the body in their contest to control those already present. It should reduce as much as possible the

flow of plasma or exudate from the burned surface or the collection of edema under it. It should also need a minimum of attention after application. Finally it should allow the natural healing processes of the body to create and maintain as nearly optimum conditions for the removal of dead tissue and for the growth of new cells as possible. This will be recognized by most readers as practically identical with the position that H. W. Orr has maintained for years in connection with infections. He has just published a fine discussion of this subject.[15]

ABSENCE OF LOCAL HARM

It is difficult in clinical studies of burns to prove whether a given treatment is harmful or not because of the impossibility of estimating accurately in all cases at the time of initial treatment the extent of the damage already done by the burns. Certainly the early return of function that has been seen in these cases immediately after removing the casts is an indication that the method is usually harmless. It is further our impression that no areas of second degree damage have been converted to third degree by this method and that epithelization takes place at a rapid rate.

A certain warning concerning the technic of application should be given, as it is theoretically possible to

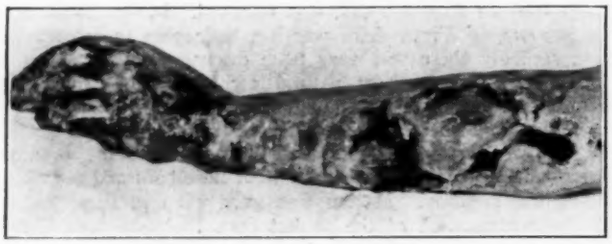


Fig. 10 (case 3).—Twenty-third day. Large areas of skin have sloughed, exposing tendons. At this time there was a surprising range of motion.

do great damage by the improper application of these casts. The cast must extend over the tips of the fingers or toes even when the burn does not, and it must not provide any zones of increased pressure at any point. Glenn, Gilbert and Drinker [11] present a photograph of a badly swollen foot when a cast was applied to the lower part of the leg of a dog without including the foot.

ABSENCE OF TOXIC ABSORPTION

Tannic acid and picric acid have been absorbed from burns treated with these materials to such an extent that liver necrosis and death have been attributed to this absorption.[15] Nothing harmful can be absorbed from the surface of burns treated with this method except the products of the burn itself or the products of bacterial invasion. Barnes and Trueta [12] have shown that absorption of foreign materials is greatly delayed from immobilized tissues. This finding is easy to understand in the light of the work of Glenn [16] and his associates, who have shown definite decreases in the flow of lymph from burns treated with casts compared with ones not thus treated. A cast also protects against reinfection from new organisms. At the same time, according to Barnes and Trueta,[12] the organisms already present either die out or become harmless. This point of view is confirmed by the experience of Cope,[13] who found a remarkable tendency for organisms to become harmless under the pressure dressings that he used.

COMFORT

From the start of treatment to complete healing the lack of pain experienced by these patients has been remarkable. As soon as the cast is applied, pain disappears. There may be a slight dull ache, experienced by 3 of the 8 patients, in the first three days. After this there is no discomfort and the arm in the cast can be moved freely. No throbbing pain, anesthesia or paresthesia has been noted. The patient can move the fingers a millimeter or so inside the cast, but this motion is painless. Removal of the cast at fourteen days is done without the aid of analgesia or anesthetic, as practically no pain results, even during the use of a cast cutter. Apparently the lack of edema or the absence of active infection in the tissues avoids the condition of extreme sensitivity to handling that is frequently seen at this time in comparable burns.

EASE OF APPLICATION

Close fitting plaster casts are relatively easy to apply, and the bulk of material (excluding water) is very little. Most doctors need no additional training in methods of applying plaster casts, although some may need encouragement before they will leave out the bulky materials customarily used in padded casts. Any man who has applied a satisfactory "skin tight" plaster to a fracture will have no difficulty at all with these casts. In our experience it is difficult for the ordinary physician to apply a Koch dressing to a burn. It necessitates quite a long experience with such dressings before a really satisfactory one is made. The bulkiness of the materials needed, especially the mechanic's waste, cellucotton or sheet wadding, may make it difficult to stock sufficient supplies where transport or storage is scanty.

LOSS OF PLASMA

The minimal subcutaneous edema in and adjacent to the burned area possible under the cast, and the small amount of surface ooze that occurs, reduce to some extent the need for plasma replacement. If the area treated by the cast is extensive, the saving should be considerable.

INFECTION

Superficial sepsis was minimal in all cases, with only a small amount of exudate present on the dressings. Cultures showed a mixture of organisms, with none predominating except in 1 case in which Pseudomonas aeruginosa was predominant. Self-limited cellulitis, unaccompanied by systemic reaction, was present in 1 case. None of the 3 patients whose burns were limited to the hands and arms developed any fever.

AFTER-CARE

During the time the cast is on, no time needs to be spent in doing dressings to the casted area. If the cast cracks from being made too thin, repair is easy. (The cast should be as thin as possible.) If the patient has to be moved during the period when the cast is on, no better protection against the normal traumas of transportation can be devised.

15. Orr, H. W.: The Physiologic Factors Involved in Protecting the Patient Against Infection in the Healing of Fractures in Compound Wounds, Tr. & Stud. Coll. Physicians Philadelphia **10**: 187-193, 1943.

16. Glenn, Peterson and Drinker.[10] Glenn, Gilbert and Drinker.[11]

HEALING

In the last analysis healing can take place only when natural defenses have created such conditions at the site of healing of temperature, p_H, salt content of the fluids, oxygen and carbon dioxide tension, nutritive elements, and enzymes that tissue cells can grow. In addition, toxic substances must be absent. Infrequency of disturbance of the environment of the injured area is therefore very important, because with each change of dressing one or more of these factors may be upset and hours or days must elapse before proper conditions can again be achieved. Under one of these casts, such disturbances of accidental nature are almost entirely prevented and those of deliberate nature (which may be just as harmful as the accidental ones, or even more harmful) such as arise from the curiosity of the doctor to see what is happening, are largely discouraged. We believe that the healing of the skin has been as rapid as in similar cases treated in other ways and that return of motion has been more rapid.

INDICATIONS FOR THIS TREATMENT

In this series, cases with burns of the hands, forearm and arms have been treated. In only 1 instance (case 2) did the burn extend above the cast. A pressure dressing was applied above this cast. There was no evidence of impairment of circulation. Zeno,[5] Afonso[6] and Trueta[7] have all used plaster casts on areas that we have not treated as yet. We are sure that this treatment is indicated for burns of the feet and legs. As we gain experience in the method we may well extend the indications more widely.

SUMMARY AND CONCLUSIONS

1. Close fitting plaster of paris casts have been used in the treatment of burns of twelve hands on 8 patients.

2. The physiologic experiments of Glenn and his associates formed the scientific background for this treatment.

3. The treatment is easy of application. The materials needed are widely available and of little bulk. Ideal protection against intercurrent infection and against the trauma of transportation is afforded.

4. The prevention of swelling and the protection provided by the treatment have resulted in comfortable rapid, uncomplicated convalescences and in excellent functional results.

ADDENDUM

Up to September 7, 14 additional patients have been treated by this method with casts applied to sixteen arms and hands, four chests and four legs. Four of the arms and hands and all the legs had third degree burns. The results of these applications of plaster have been very satisfactory.

319 Longwood Avenue.

By-Products from Sewage.—Trucks rumbling through the streets of oil starved Germany today are operating on methane gas, obtained as a by-product from municipal sewage treatment plants. In Bradford, England, sewage disposal processes are yielding 500 tons weekly of vitally needed grease. In the United States a big steel plant is buying huge quantities of liquid effluent from a city sewage plant because existing industrial water supplies are inadequate to meet expanded output. These three examples dramatize what might be considered the ultimate in deriving salvage from waste. They focus attention on one of the least suspected sources of valuable "by-products"—the city sewage disposal system.—Cleary, Edward J.: Dollars from Sewers, *Scientific American*, September 1943, p. 106.

Clinical Notes, Suggestions and New Instruments

FAILURE OF NEPHRECTOMY TO INFLUENCE HYPERTENSION IN UNILATERAL KIDNEY DISEASE

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Experimental production of hypertension by partial occlusion of the blood supply to one kidney [1] has suggested that intrinsic unilateral renal disease in man can similarly cause arterial hypertension. The acceptance of this thesis has led to the search for unilateral disease in hypertensive patients and, when found, to nephrectomy of the suspected kidney. Seventy-six published case reports of attempts to cure hypertensive disease in man by removal of a diseased kidney have been reviewed in detail by Smith, Goldring and Chasis.[2] In the opinion of

Pyelonephritic left kidney weighing 33 Gm.

these authors, in only 7 of the 76 patients has nephrectomy been successful in reducing the elevated blood pressure to the normal range.

It has been argued that failure to reduce the blood pressure in a patient with a long-standing unilateral kidney disease and hypertension might be explained on the basis of irreversible vascular changes in the remaining kidney capable of maintaining the hypertensive process. This report is made because nephrectomy failed to reduce the blood pressure of a patient in whom postoperatively the remaining kidney is not diseased and has a normal blood flow per unit of functioning renal tissue.[3]

From the Department of Medicine, Temple University Medical School, Philadelphia, and the Department of Physiology, New York University College of Medicine, New York.

1. Goldblatt, Harry; Lynch, James; Hanzal, R. F., and Summerville, W. W.: Studies on Experimental Hypertension: I. The Production of Persistent Elevation of Systolic Blood Pressure by Means of Renal Ischemia, J. Exper. Med. **59**: 347 (March) 1934.

2. Smith, H. W.; Goldring, William, and Chasis, Herbert: Is Essential Hypertension of Renal Origin? Bull. New York Acad. Med., to be published.

3. Smith, H. W.; Goldring, William, and Chasis, Herbert: The Measurement of the Tubular Excretory Mass, Effective Blood Flow and Filtration Rate in the Normal Human Kidney, J. Clin. Investigation **17**: 263 (May) 1938.

REPORT OF CASE

History.—S. H., a white woman aged 34, seen in October 1941, complained of high blood pressure, headache and slight fever. She had been in good health until a year and a half before, when her fourth and last child was born. Following delivery she had a fever which lasted three weeks, and during this time there were occasional chills. For about six months she was relatively well, and then she began to feel weak and listless. She complained of headaches in the temporal region, described as dull, and at the top of the head, described as burning. Other aches and pains had been present and she also suffered from insomnia. The temperature and blood pressure were both found to be slightly elevated.

There were no other serious illnesses in the previous history. After the third pregnancy five years before there had been a febrile illness diagnosed as a "slight touch of pneumonia." The patient had been ill for only a week and was quite well afterward. The systemic review disclosed nothing of importance.

She did not know of any history of hypertension or cardiovascular renal disease in her family.

Unconscious feelings of guilt and hostility seemed to be important features of her personality. Outwardly passive and pleasant, inwardly she exhibited a great deal of resentment toward her husband and her mother.

Effective Renal Blood Flow, Glomerular Filtration Rate and Maximal Tubular Excretory Capacity Before and After Left Nephrectomy

	Renal Plasma Flow (C_D) Cc. per Minute	Filtration Rate (C_{In}) Cc. per Minute	Maximal Tubular Excretory Capacity (T_{mD}) Mg. Iodine per Minute	Renal Plasma Flow / Max. Tub. Exeret. Cap. (C_D/T_{mD})
	Preoperative Observations—March 23, 1942			
Right kidney	386.2	84.2	45.4	8.5
Left kidney	55.7	17.0	3.0	18.4
Total	441.9	101.2	48.4	9.1
	Postoperative Observation—June 5, 1942			
Right kidney	592.6	95.8	48.4	12.2
Normal *	594 ± 102.4	117 ± 15.6	42.6 ± 9.46	14.2 ± 2.36

* The diodrast clearance was used to measure the effective renal blood flow,[5] the mannitol clearance to measure the rate of glomerular filtration,[4] and the diodrast saturation method to determine the maximal tubular excretory capacity.[5] Values given at the bottom of the table are based on observations in normal female subjects.

Physical Examination and Laboratory Studies.—The general physical examination did not disclose any abnormalities. Gynecologic examination was negative. The eyegrounds showed mild attenuation of the retinal arterioles. There was no evidence of arteriosclerosis and no retinitis. There was moderate elevation of blood pressure, which varied between 150 to 170 systolic and 90 to 120 diastolic. There was an occasional slight elevation of the temperature to 99.3 F. Urinalysis and Wassermann tests were negative and the blood count was normal. The sedimentation rate was 14 mm. and the basal metabolic rate was minus 6 per cent.

Culture of the urine showed many coliform bacilli, and an intravenous urogram showed that the left kidney was much smaller than normal with a deformity of the calices which suggested pyelonephritic contraction. The right kidney was larger than normal and presented a normal appearance.

Retrograde pyelography of the left side was then done, and this showed irregular and distorted major and minor calices which suggested a cicatricial deformity. This was in keeping with the diagnosis of chronic pyelonephritis. The same type of organism was obtained from direct culture of the left kidney.

The patient was placed on sulfathiazole medication, and the Addis count showed a slight excess of white blood cells and many sulfathiazole crystals. Medication was then changed to sulfadiazine, which was well tolerated. Cultures of the urine following the administration of sulfadiazine were negative.

The patient was studied again in December 1941. The blood pressure was higher than before, 185/135. Slight fever (99.5 F.) continued. A left retrograde pyelogram was the same as before. Culture of the urine was negative.

Operative Findings.—A small left kidney weighing 33 Gm. was removed in April 1942 (shown in the illustration). The capsule was thin and stripped with ease. The capsular surface was definitely lobulated. The cut surface of the kidney showed a normal relationship of cortex and pyramids. The pelvic mucosa seemed of normal thickness and there was no gross evidence to sugest inflammation or scarring. The larger blood vessels showed nothing abnormal on gross examination. The lining was smooth and the contents resembled old blood.

Sections of the kidney were studied by Dr. E. E. Aegerter and by Dr. Irving Graef. It was agreed that the scarring was of the type commonly seen in healed or chronic pyelonephritis. This was confirmed by microscopic examination, which showed that the indentations were the result of scarring typical of the late stage of pyelonephritis.

The glomeruli seemed almost normal in appearance and number. There were 47 glomeruli in a low power field compared with 62 in a normal adult kidney. Individual glomeruli showed no replacement fibrosis or reduction in size. There was no patchy cortical atrophy or failure of development of the tubules. There was arteriosclerotic involvement of the medium sized branches of the renal artery and hypertrophy of the afferent arterioles.

The section which included the pelvis and calices showed rich lymphocytic infiltration beneath the epithelium. The tubular remains in the scarred areas also exhibited the typical dilatation and colloid type of cast seen in pyelonephritic scars.

Postoperative Course.—Following the operation the blood pressure was even higher than before, with levels of 170 to 200 systolic and 120 to 140 diastolic. The patient was seen about every two months. The last observation was in April 1943, twelve months after the operation. Symptoms were no different, although there had been a slight gain in weight. She "loses one ache and gets another." Fatigue and shortness of breath (sighing respirations) were now a prominent part of the clinical picture. It was concluded that the occasional slight rise of temperature did not indicate infection but was normal for the patient.

The glomerular filtration rate,[4] the effective renal blood flow [5] and the maximal tubular excretory capacity [5] were measured in the separate kidneys preoperatively and in the remaining right kidney postoperatively.[6] The results of these observations are presented in the accompanying table.

COMMENT

The preoperative observations on this patient revealed extreme functional impairment of the left kidney. The glomerular filtration rate, effective renal blood flow and maximal tubular excretory capacity were definitely reduced. The functional size of the diseased kidney was approximately one-seventh the normal kidney. These measurements also indicated the presence of a large number of impotent nephrons, that is, nephrons which had lost their excretory power but continued to act as conduits in conveying urine to the collecting tubules.

The glomerular filtration rate, the effective renal blood flow and the maximal tubular excretory capacity in the right kidney was increased above one half the mean normal value. This was interpreted as indicating hypertrophy of the right kidney, the stimulus probably being long-standing disease of the contralateral kidney. The ratio of renal blood flow to tubular excretory capacity, which expresses the amount of blood going to functioning tubular tissue, was decreased, indicating relative ischemia in this hypertrophied right kidney.

Postoperatively the right kidney shows an increase in effective renal blood flow, glomerular filtration rate and maximal tubular excretory capacity; this one kidney, functionally speaking, is now the equal of two normal kidneys. The ratio of blood flow to functional tubular tissue is now in the normal range.

4. Smith, W. W.; Finkelstein, Norma, and Smith, H. W.: Renal Excretion of Hexitols (Sorbitol, Mannitol and Dulcitol) and Their Derivatives (Sorbitan, Isomannide and Sorbide) and of Endogenous Creatinine-like Chromogen in Dog and Man, J. Biol. Chem. **135**: 231 (Aug.) 1940.

5. Goldring, William; Chasis, Herbert; Ranges, H. A., and Smith, H. W.: Relations of Effective Renal Blood Flow and Glomerular Filtration to Tubular Excretory Mass in Normal Man, J. Clin. Investigation **19**: 739 (Sept.) 1940.

6. Chasis, Herbert, and Redish, Jules: Function of the Separate Kidneys in Hypertensive Subjects, Arch. Int. Med. **70**: 738 (Nov.) 1942.

The persistence of hypertension in this patient postoperatively indicates that the unilateral atrophic pyelonephritis was not causally related to the hypertensive process. Furthermore, the fact that the renal blood flow per unit of functioning tissue is in the normal range in the remaining kidney excludes the possibility that chronic irreversible vascular changes resulting in ischemia of this kidney is maintaining the abnormal elevation of blood pressure: the fact that the hypertensive process was of relatively short duration strengthens this view. It appears that the intrinsic unilateral disease present in this patient was not the cause of the arterial hypertension.

CONCLUSION

The removal of a chronic atrophic pyelonephritic kidney failed to lower the blood pressure of a hypertensive patient. The remaining kidney cannot be indicted for this failure, since it is neither diseased nor ischemic. It is concluded that the intrinsic unilateral renal disease in this patient was not causally related to the arterial hypertension.

269 South Nineteenth Street—44 East Sixty-Seventh Street.

THE USE OF HUMAN FIBRINOGEN IN RECONSTRUCTIVE SURGERY

COMMANDER PAUL MICHAEL, MC-V (S), U.S.N.R.
AND
LIEUT. COMDR. WALTER ABBOTT, MC-V (S), U.S.N.R.

The successful application of the principles involved in the use of human fibrinogen is thought of sufficient and timely interest to report at this time. Work on animals has proved that both bovine and human fibrinogen may be used to good advantage as a bridge for tissue regeneration. The present case report presents the successful use of this substance in the treatment of a human patient.

REPORT OF CASE

History.—P. B., a man aged 27, was injured by a high explosive fragment on Nov. 19, 1942, sustaining a laceration of the right thigh. He developed a foot drop with paresthesias over the outer aspect of the thigh and foot. A month later he complained of a severe burning pain in the foot. X-ray examination revealed a foreign metallic body in the soft tissues at the middle third of the thigh. On March 23, 1943 a small

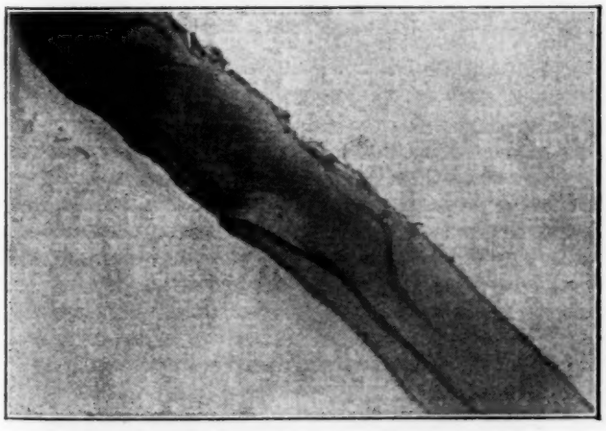

Fig. 1.—Microscopic section (× 150) taken through the fibrinogen after being used in the body for over four weeks. There is very little inflammatory reaction and no evidence of absorption of the fibrinogen.

piece of shell fragment measuring 1.0 by 0.7 cm. was removed from the sciatic nerve and because of the denuded sheath human fibrinogen film was applied. (Fibrinogen was supplied to Comdr. R. R. Mazet (MC), U.S.N.R., by the Physiologic Laboratory, Harvard University). The film of fibrinogen was wrapped round the nerve and six weeks later the operative site was opened and the film removed. At this time healthy nerve tissue was observed with an excellent healing process in progress. The pain in the foot now had subsided.

Pathologic Examination.—The first specimen received in the laboratory (March 23, 1943) consisted of a piece of metal measuring 1.5 by 0.7 cm. Also present were several irregular

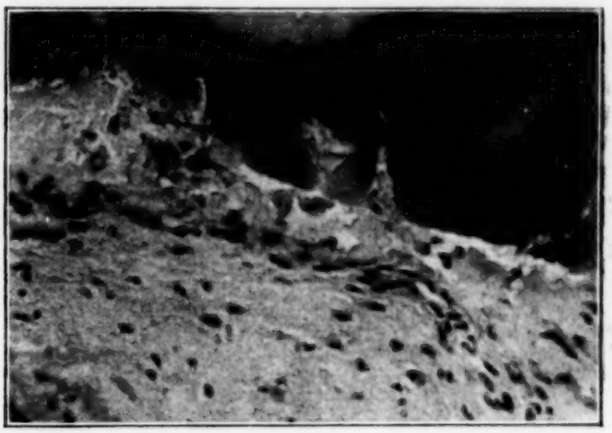

Fig. 2.—Section (× 500) taken through the nerve sheath with attached fibrinogen on the surface. Note the glassy homogeneous structure of the fibrinogen with no apparent irritation. The nerve sheath shows a normal growth. Note the absence of any foreign body reaction in the tissue.

small fragments of gray tissue said to be removed from the sheath of the sciatic nerve.

On microscopic examination the fragments were seen to consist of dense fibrous connective tissue in which were large collections of amorphous hyaline refractile granular pigment. These pigment granules were surrounded by whorls of hyperplastic fibrocytes and lymphocytes and occasional giant cells. The adjacent muscle fibers did not appear to be involved in the process.

The diagnosis was granulation tissue, nerve sheath; foreign body reaction (high explosive fragment).

The pathologic report on the second operation (April 24) was as follows:

Gross: The submitted specimen consisted of a small pearly white glistening fragment of tissue removed from a nerve sheath, measuring 1 by 0.5 mm., a small mass of muscle measuring 1 by 0.8 cm., and some thin sheets of fibrinogen measuring 3 by 1.5 cm. These were sectioned for microscopic study.

Microscopic: The microscopic sections taken from the fibrinogen showed glassy amorphous structure with a pronounced acidophilic staining reaction. There was very little in the way of evidence which would suggest an irritation reaction from this substance. The nerve sheath showed some clearcut fibrinogen on the surface with a few round cells and fibroblasts in the sheath but very few neutrophilic polymorphonuclear cells or other indications of irritation.

The diagnosis was fibrinogen; nerve sheath fragment.

COMMENT

From the description it may be said that the fibrinogen placed around the sciatic nerve on March 23 gave little evidence of tissue irritation. A small section of nerve sheath revealed evidence of growth of a rather normal nature. There was no evidence of any foreign body reaction in the usual sense of the word, and the fibrinogen showed little in the way of absorption. There was no evidence of inflammatory cells in the fibrinogen.

CONCLUSIONS

The application of this substance opens up many new possible uses in reconstructive surgery, especially in neurosurgery and tendon repair work. The microscopic sections of the nerve sheath and fibrinogen after removal show the lack of irritation or foreign body reaction, yet healing has gone on normally. This procedure may be adapted to meet other needs in reconstructive surgery.

This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the U. S. Navy. The opinions and views set forth in this article are those of the writers and are not to be considered as reflecting the policies of the Navy Department.

Special Article

HANDBOOK OF NUTRITION: XXIV

NUTRITION IN PREVENTIVE MEDICINE

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These special articles on foods and nutrition have been prepared under the auspices of the Council on Foods and Nutrition. The opinions expressed are those of the authors and do not necessarily reflect the opinion of the Council. These articles will be published later as a Handbook of Nutrition.—ED.

The prevention of malnutrition and the deficiency diseases is probably the greatest and most complex problem in public health that this country has ever had. The exact extent of physical disability, economic loss and disease directly or indirectly related to nutrition are unknown, and yet there is every indication that malnutrition is very widespread. Some physicians who do not see many cases of advanced deficiency disease feel that the importance of nutrition is being overemphasized. However, in every clinic in which close observations are made and the more refined methods of diagnosis used, many unsuspected cases of malnutrition are recognized, and every study reveals the importance of mild degrees of deficiency in producing symptoms the cause of which was hitherto unrecognized. Furthermore, it is significant that almost all practicing physicians are prescribing vitamin preparations for more and more of their patients.

Even before our food supply was disturbed by the conditions incident to war, a number of surveys had all shown that a large part of our population was eating foods which failed to provide the essentials in amounts recommended for optimum nutrition. For example, a survey of the diets of more than a thousand workers in a large aircraft factory [1] revealed that more than four fifths of the diets studied fell below the amounts of certain nutrients recommended by the Food and Nutrition Board of the National Research Council.[2] Nutritionists who have watched workers select their lunches in cafeteria lines report that not more than half of them choose good lunches even when foods needed to provide good lunches are on the counters. It was also observed that women usually made poorer choices than men. The method of food preparation also greatly affects its food value. In a study of food as it was served [3] it was shown that as much as 90 per cent of the thiamine (B_1) present in the fresh raw food was lost before the food was eaten. Keeping food hot for long periods of time is really overcooking it, and the vitamins destroyed by heat and oxidation are thus lost. The hot lunch prepared and kept hot for hours before consumption may not be as satisfactory nutritionally as a cold one.

The effect of such inadequate diets on the ability of the civilian worker to do his part in the war effort must be of serious concern to us at this time. As a nation we are not as well fed as we once believed. Physicians and health officers must recognize that here is a whole new sphere of responsibility in the field of preventive medicine as great as or greater than the field of sanitation or control of communicable diseases.

The growing recognition of the importance of nutrition in health has gone hand in hand with the development of the science of nutrition. Most of what may be called the modern knowledge of nutrition has developed during the present century and much of it since World War I. The discovery of new vitamins, the recognition of the great physiologic importance of various mineral salts and better methods of diagnosis have made the entire world increasingly aware of the enormous amount of ill health, poor development, disease and disability due either directly or indirectly to malnutrition. An indication of the extent of the problem is given just by a survey of the fragmentary reports in the medical literature on the prevalence of the vitamin deficiency diseases.

The principal dietary deficiency diseases are nutritional edema, vitamin A deficiency, vitamin D deficiency, vitamin B_1 (thiamine) deficiency, nicotinic acid deficiency (pellagra), riboflavin deficiency (ariboflavinosis), vitamin C deficiency (scurvy) and vitamin K deficiency. These diseases occur to some extent throughout the world, although there are frequently wide variations in geographic distribution.

Although reports in many instances indicate an extensive occurrence of deficiency disease, they most probably represent only a small proportion of the cases actually occurring in the world.

NUTRITIONAL EDEMA

Nutritional edema is an invariable accompaniment of famine and rapidly disappears when the patient is given enough food of good quality. Together with the prolonged undernutrition a deficiency of protein appears to be the most important factor in the production of this syndrome, although it is recognized that strenuous exercise, exposure to cold and probably other influences are contributory.

In mild cases the edema may be confined to the lower limbs, but when it is more severe it extends to all parts of the body. It is accompanied by emaciation, muscular weakness, depression, anemia and very frequently gastrointestinal disturbances. The swollen extremities are cold and painful when touched, the pulse is slow and the blood pressure is low.

This disease is very common in prison camps and during periods of famine. It has been especially prevalent in India and in China. During the latter years of the first world war it reached epidemic proportions among the poorer classes of the civilian populations of the central European countries. In Bohemia alone 22,842 cases were listed. In the Russian famine of 1921-1922 every single surviving inhabitant of certain towns was affected. During the present nutritional crisis in Europe and in China we may be certain that the incidence of nutritional edema is extremely high although no accurate figures are as yet available.

VITAMIN A

Vitamin A deficiency is manifested in human beings by lesions found chiefly in the epithelial structures. The most readily recognized symptoms are those of the severe deficiency states. Xerophthalmia is associated with atrophy of the paraocular glands, hyperkeratosis of the conjunctiva and finally involvement of the cornea leading to softening or keratomalacia and blindness.

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Nyctalopia, or night blindness, is due to a functional failure of the retina in the proper regeneration of visual purple. The characteristic skin lesions were first recognized in Chinese soldiers in 1931.[4] The lesions consist of epidermal hyperplasia and glandular atrophy and are represented by papular eruptions around the pilosebaceous follicles. Unlike the ocular manifestations, cutaneous eruptions occur in persons between 16 and 30 years of age and not in infants. It is common among men, and 90 per cent of those showing the dermatosis have obvious ocular manifestations of vitamin A deficiency.[5]

The symptoms of milder deficiency states are more difficult to detect. Early stages of conjunctival xerosis occur which may be discovered only by biomicroscopic examination.[6] Incipient night blindness may be demonstrable only by careful studies of dark adaptation for which a variety of photometric instruments and technics have been introduced. Mild dermatoses resembling the more florid eruptions of advanced vitamin A deficiency and responding to treatment with vitamin A preparations have been described.[7] Levels of carotene and vitamin A in the blood and tissues have been determined in an effort to use them as criteria of deficiency states, either manifest or subclinical. Vitamin A has also been given a role in disorders of the respiratory tract,[8] genitourinary tract,[9] central nervous system,[10] teeth,[11] thyroid gland [12] and other organ systems and structures.

Xerophthalmia and nyctalopia have been reported from almost every part of the world. In most countries it is infrequent except under unusual circumstances. It is prevalent, however, in India,[13] China,[14] the Dutch East Indies,[15] other Asiatic areas,[16] British Guiana [17] and sections of Africa.[18] A study in South India [19] in 1937 found as many as 15 per cent of 4,000 school children showing xerophthalmia and keratomalacia. In Bengal [20] xerophthalmia and nyctalopia were found in 9 per cent of 2,000 persons. In Tientsin, China,[21] a survey of school children uncovered the presence of xerophthalmia in 83 per cent of certain groups. Five per cent of children admitted to a Batavia hospital [22] were xerophthalmic, and in Groot-Atjeh [23] it was found to be "widespread." In Ceylon [24] 65 per cent of the blindness was attributable to xerophthalmia, the latter being noted as "common." Of 500,000 persons in Java [25] about 1 per cent of blindness was found, and here too xerophthalmia was the chief cause. In Sumatra [26] 20 to 61 per cent of 3,684 children showed evidences of xerophthalmia, and in 1939 1 per cent of 8,677 children examined in the Philippine Islands [27] had this disease. In 1937 keratomalacia, xerophthal-

TABLE 1.—*Reports of Occurrence of Nutritional Edema*

Area	Year	Incidence or Number of Cases Reported	Comment	References
United States (South)	1942	15% of hospital patients	.....	The Food and Nutrition of Industrial Workers in Wartime, Nat. Res. Council Reprint and Circular Series No. 110, April 1942
United States (Tennessee)	1941	Relatively small number	900 people studied; 20% of adults had hypoproteinemia	Youmans: Am. J. Pub. Health **31**: 704, 1941
United States	1936	41 cases	9 years' observation	Dodd and Minot: J. Pediat. **8**: 442, 1936
United States	1936	Not now common	Possibly increased during first years of depression	McLester: J. A. M. A. **106**: 1865, 1936
India (Rangoon)	1934	Increasing	With increasing trade depression	Kundu: Indian M. Gaz. **69**: 439, 1934
China	1942	130 children, 14%	Of 903 patients admitted to hospital	Chen: Am. J. Dis. Child. **63**: 552, 1942
China (Manchuria)	1937	21 cases	.....	Doi: J. Orient. Med. **27**: 115, 1937
Spain	1942	12%	Of 270 persons	Robinson, Janney and Grande: J. Nutrition **24**: 557, 1942
Spain	1940	One of 5 main deficiency diseases	3,116 people studied; 64% of women and 36% of men had a deficiency disease	Jiminez Garcia and Grande Covian: Rev. clin. española **1**: 41, 313, 318, 323, 1940
Netherland East Indies	1940	Cases reported	Due to failure of harvests of 1937 and 1938	Streef, Streef Spann and Ismangil: Geneesk. tijdschr. v. Nederlandisch-Indië **80**: 990, 1940
East Africa (Kenya)	1938	12 cases	April to October, 1937	Bell: East African M. J. **14**: 327, 1938
Egypt	1938	18 infants	.....	Shukry, Mahdi and El Gholmy: Arch. Dis. Childhood **13**: 254, 1938
Uganda	1939	Considerable in prisons up to about 1934	.....	Report of Committee on Nutrition for British Colonial Empire, 1939
Northern Rhodesia	1939	Reported	.....	
British Honduras	1939	Reported	.....	
Fiji	1939	Reported	.....	
Sierra Leone	1939	Extensive in prisons, barracks and asylums	.....	
Bechuanaland	1939	Frequent	.....	
Leeward Islands (Antigua)	....	Not uncommon	.....	

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TABLE 2.—*Reports of Occurrence of Vitamin A Deficiency*

Country and Year	Deficiency Symptom	Incidence	Groups Studied	References
		NORTH AND SOUTH AMERICA		
New Foundland, Labrador..... 1939-1940	Xerophthalmia, 0; dark adaptation, 9%; nyctalopia, 3%	"Probably more extensive use of controlled procedures will show that even very mild vitamin A deficiency ordinarily is rare in occidental population"	353 adults	Steven and Wald [46]
Canada (Edmonton)..... 1939	Dark adaptation, 24%	Evidence of vitamin A deficiency	1,000 university students	Pett [53]
United States (Kansas)..... 1942	Clinical evidence	None	1,265 workmen	Schnedorf, Weber and Clendening [44]
United States (Chicago)..... 1942	Dark adaptation, blood levels	"Mild deficiency is rare or not detectable by these methods"	Children	Oldham, Roberts, MacLennan and Schlutz [63]
United States (New York City).. 1941	Biomicroscopic, slit lamp examination	86.6% showed evidence of vitamin A deficiency	Poor school children	Wiehl and Kruse [6]
United States (California)..... to 1942	Clinical deficiencies	None	385 hospital patients	Krupp [44]
United States (general)..... to 1941	Xerophthalmia	One case in several years reported in literature	.....	Youmans and Patton [44]
United States (general)..... to 1941	Nyctalopia, dermatosis, anatomic changes, "mild deficiency"	"Not uncommon"	.....	Youmans and Patton [44]
United States (North Carolina). 1940-1941	Clinical deficiencies Blood level at lower limits	None "Common"	Mill village community of 400	Milam [44]
United States (Tennessee)..... 1941	Dark adaptation	"High incidence" of vitamin A deficiency	900 rural people	Youmans, footnote 52, first reference
United States (Florida)..... 1941	Follicular conjunctivitis	21.7% had vitamin A deficiency	1,041 school children	Sandels, Cate, Wilkinson and Graves [62]
United States (New York City).. 1940	Dark adaptation	One case	144 children	Lewis and Haig [64]
United States (Tennessee)..... 1938	Dark adaptation	50% showed vitamin A deficiency	54 adults in Nashville	Corlette, Youmans, Frank and Corlette [55]
United States..... to 1937	Dark adaptation	35% showed vitamin A deficiency	Medical students	Jeghers [52]
United States..... to 1937	Dark adaptation	50% showed vitamin A deficiency	Clinic patients	Youmans, footnote 52, second reference
United States (Iowa)..... to 1936	Dark adaptation	26 to 79% showed vitamin A deficiency	Children	Jeans, Blanchard and Satterthwaite [54]
Brazil..... 1932-1933	Nyctalopia	"A number of cases were observed during a period of drought"	General population	Cavalcanti [47]
British Guiana..... 1938	Xerophthalmia, nyctalopia	"Common"	.....	Footnote 17
Yucatan and Labrador..... to 1937	Xerophthalmia, nyctalopia	"Common"	General population	Eddy and Dalldorf [45]
United States (general)..... to 1934	Xerophthalmia	"Rare"	.....	Thorson: J. A. M. A. **103**: 1438 (Nov. 10) 1934
Trinidad..... 1941	Xerophthalmia, nyctalopia	"Rare"	.....	Metivier [48]
		EUROPE		
England..... 1940	Hyperkeratosis	5% had this evidence of vitamin A deficiency	General population	Pemberton [50]
England (Newcastle upon Tyne) 1938-1939	Clinical deficiencies	None	138 (poor income group) children	Brewis and others [34]
France (Marseilles)..... 1941	Clinical deficiencies; "Laboratory data indicating mild deficiencies"	None Widespread	Several hundred of school children and general population	Youmans [36]
France..... 1940	Total deficiency, partial deficiency (Dry skin, digestive disturbance, nyctalopia, irritability)	Rare Prevalent	Adults and children	Chevallier [34]
France..... to 1939	Xerophthalmia	Only 7 cases described to date	General literature	Clement and Delon [35]
France (Paris) 1940-1941	Xerophthalmia	Same as before (?)	In hospitals	Minoli [34]
France..... 1938	Dark adaptation	"Relatively frequently"	210 school children	Caussade and others [57]
Spain (Madrid)..... 1941	Nyctalopia, 2%; dermatosis, 13%; blood level at or below borderline 33%	Evidences of vitamin A deficiency	106 families or 561 persons	Robinson, Janney and Grande Covian [38]
Italy (Turin)..... 1939	Nyctalopia	45% showed this vitamin A deficiency	500 school children	Mathis [39]
Italy (Venice)..... 1939	Low blood levels, nyctalopia	Frequent incidence of these vitamin A deficiencies	.....	Bretti and Tria [40]
Italy (Venice)..... 1939	Nyctalopia	"Common" occurrence of this vitamin A deficiency	Children	Tria [40]
Czechoslovakia (Prague)..... 1938	Clinical deficiencies	"No serious deficiency (vitamin A) but a slight lack of the vitamin was indicated by dry affections of the skin and nyctalopia"	Replies to 1,218 questionnaires sent to health officers	Charvat [42]
Sweden (Djuroholm)..... 1939	Dark adaptation	28% showed this vitamin A deficiency	67 school children	Abramson and Örgaard [58]
Finland (Helsinki)..... 1940	Dark adaptation	29% showed this vitamin A deficiency	71 persons	Nylund [59]

TABLE 2.—*Reports of Occurrence of Vitamin A Deficiency—Continued*

Country and Year	Deficiency Symptom	Incidence	Groups Studied	References
		EUROPE—Continued		
Finland (Helsinki)..... 1938-1940	Dark adaptation	16.2% showed this vitamin A deficiency	1,377 persons	Simola and Saksela [59]
Denmark (Copenhagen)..... 1937	Dark adaptation	2.4% "uncommon"	332 hospital patients	Mowinckel-Reistrup and Reiter [58]
Denmark (Copenhagen)..... 1935	Dark adaptation	71% showed this vitamin A deficiency	65 children	Frandsen [56]
Germany (Posen)..... 1942	Dark adaptation	None	173 persons	Widenbauer [60]
Germany (Halle)..... 1939	Nyctalopia	17% showed this vitamin A deficiency	218 persons	von Drigalski and others [43]
Sweden, Norway, Finland, Czechoslovakia, Yugoslavia, 1939	Nyctalopia, dermatosis	"Frequently reported"	Rural population	Bull. Health Organ.[61]
Egypt (Cairo)..... 1938	Xerosis of conjunctiva and cornea, nyctalopia	0.4% 0.2%	Patients in general ophthalmic hospital	Giza Memorial [31]
Tanganyika Territory..... 1939	Dark adaptation, nyctalopia 10%	93% showed this vitamin A deficiency	94 native patients and convicts; school boys	McKenzie [29]
Uganda (Teso)..... 1935	Xerophthalmia, phrynoderma	300 cases, 30% in children, 8.7% in adults	1,112 persons	Loewenthal [30]
Union of South Africa..... 1942	Keratomalacia, Bitôt's spots Phrynoderma	None "Considerable number"	841 children	Brock and Latsky [32]
Falkland Islands..... 1937	Xerophthalmia	None	.....	Annual report [48]
		ASIA		
India (Calcutta)..... 1941	Dark adaptation, nyctalopia	6% of these vitamin A deficiencies	138 persons	Roy and Bauergee [61]
India (Calcutta)..... 1941	Lesions from nyctalopia to xerophthalmia	3%	14,698 persons in eye infirmary	Kirwan, Sen and Biswas [13]
India (Bengal)..... 1941	Xerophthalmia, nyctalopia	9%	2,000 persons	Biswas [20]
India (Bengal)..... 1941	Dark adaptation	"27% were below standard"	391 school boys	Basu and De [61]
India (general)..... to 1937	Xerophthalmia, nyctalopia	"Common"	General population	Eddy and Dalldorf [45]
India (Kashmir)..... 1939	Phrynoderma	10% showed this vitamin A deficiency	Children	Nicholls and Nimalasuriya [49]
South India..... 1937	Xerophthalmia, keratomalacia	Up to 15%	4,000 school children	League of Nations [19]
China..... to 1937	Xerophthalmia, nyctalopia	"Common"	General population	Eddy and Dalldorf [45]
China (Tientsin)..... 1929-1930	Xerophthalmia	Eye clinic patients 6%, charity boarding schools 83%, poor vernacular schools 29%, upper class schools 3%, mental asylums 44%, mental asylums (Europe) 2%	.....	Nicholls [21]
Malaya (Singapore)..... 1938	Xerophthalmia	"Not uncommon"	Children	Malaya Journal [16]
Dutch East Indies (Batavia).... 1935-1940	Xerophthalmia	5%	Children admitted to hospital	De Haas and others [22]
Dutch East Indies (Groot-Atjeh) 1937	Xerophthalmia	"Widespread"	.....	Gomperts [23]
Dutch East Indies (Batavia).... 1937-1939	Dark adaptation	60 to 80% showed this vitamin A deficiency	430 persons	Gorter [62]
Dutch East Indies..... 1938	Xerophthalmia	1.3%	3,000 children under 15 years	Hadikoesoemo [18]
Dutch East Indies..... 1937	Xerophthalmia, keratomalacia, nyctalopia	"Common"	.....	League of Nations Conference [28]
China..... 1937	Xerophthalmia, keratomalacia	"Common"	.....	
British Solomon Islands..... 1937	As above	"Common"	.....	
New Hebrides (Condominium).. 1937	As above	"Unknown"	.....	
Tonga Islands..... 1937	As above	"Exists"	.....	
Fiji Islands..... 1937	As above	"Almost complete absence"	.....	
Dutch East Indies (W. Java).... 1939	Xerophthalmia	About 1% blindness, of which xerophthalmia is chief cause	500,000 persons	Tijssen [25]
Dutch East Indies (Sumatra)... 1939	Xerophthalmia (mild and severe)	38% to 2 years; 51-61%, 2-15 years; 20%, 15 years	3,684 children	Maäs [26]
Ceylon (Southern)..... 1939	Phrynoderma, Bitôt's spots	21% 5.6%	976 children 1,497 children	Nicholls and Nimalasuriya [49]
Ceylon (Northern).....	Bitôt's spots	Less than above	.....	Nicholls and Nimalasuriya [49]
Ceylon..... 1937	Xerophthalmia	65% of blindness caused by xerophthalmia	.....	League of Nations [24]
Ceylon..... 1937	Xerophthalmia	"Common"	Prisoners	Ceylon Sessional Papers [15]
Philippine Islands..... 1939	Xerophthalmia	1%	8,677 persons	Ubaldo and de Campo [27]
Philippine Islands..... 1927-1937	Keratomalacia	47 cases noted	Pediatric service of General Hospital in children—5 yrs.	Tupas and Pecache [10]

mia and nyctalopia were reported as "common" in the British Solomon Islands,[28] as "unknown" in the New Hebrides Condominium,[28] as "existing" in the Tonga Islands [28] and "almost completely absent" in the Fiji Islands.[28]

Reports [29] from Tanganyika Territory in 1939 showed 10 per cent of the school boys to be suffering from night blindness. In Teso, Uganda,[30] a 30 per cent incidence of xerophthalmia was found among children in a group of 1,112 persons of all ages. In Cairo, Egypt,[31] only 0.2 per cent of persons attending a general ophthalmologic hospital were nyctalopic, and 0.4 per cent showed xerosis of the conjunctiva and cornea. No cases were found in a thorough 1942 survey of 841 children in the Union of South Africa [32] and none were noted in the Falkland Islands.[33]

In Europe, xerophthalmia is uncommon.[34] Up to 1939 only 7 cases had been reported in the French medical literature,[35] and reports up to 1941 [36] failed to add any further cases. Under unusual circumstances the disease appeared in epidemic form, as in Denmark [37] during World War I, when dairy products were replaced in the diet by fats lacking in vitamin A. A recent survey of 106 families including 561 persons in Madrid, Spain,[38] uncovered only 2 per cent with nyctalopia. In Italy, however, the incidence is reported to be much higher. In Turin in 1939 [39] 45 per cent of 500 school children had night blindness, and it was also found to be common in Venice.[40] A study of rural populations [41] revealed that nyctalopia and dermatosis were "frequently reported" from Sweden, Norway, Finland, Czechoslovakia and Yugoslavia. A year earlier, in 1938, a report [42] from Prague based on a questionnaire survey found no serious deficiencies, although dermatoses and nyctalopia were noted. In Halle, Germany,[43] in 1939 17 per cent of 218 persons were found to be night blind.

In the United States [44] xerophthalmia, keratomalacia and nyctalopia due to vitamin A deficiency are rarities. In Yucatan [45] and British Guiana [17] they are reported as "common." A recent study in Newfoundland and Labrador [46] uncovered no cases of xerophthalmia and only 3 per cent of night blindness among 353 adults. In Brazil [47] a number of cases of nyctalopia were noted during a period of drought. The conditions were reported from Trinidad [48] as of "rare" occurrence.

The severe dermatoses of vitamin A deficiency are found in the same geographic distribution as the advanced ocular manifestations. Reports from China [8] and other countries [49] indicate the incidence of this symptom to be as high as or higher than that of ocular symptoms. The occurrence of mild dermatoses as evidence of low grade vitamin A deficiency has been reported widely. Five per cent of a general population group in England [50] in 1940 showed such a hyperkeratosis, and 13 per cent of a similar group in Madrid, Spain,[38] in 1941 had such lesions. It has been frequently reported from the Scandinavian countries,[41] central Europe,[51] Asia [49] and South Africa.[32]

The failure of the eye to adapt properly to darkness has been reported as a mild vitamin A deficiency symptom and has been subjected to refined biophotometric measurement. Reports of such studies have been at variance as the result of the multitude of technics and instruments employed, the failure to consider other etiologic factors of dysadaptation and the unavailability of universally accepted criteria of subclinical vitamin A deficiency disease to serve as standards.

A high incidence of dark dysadaptation has been reported widely in the United States [52] and throughout the world.[53] Among 120 Iowa school children [54] almost 20 per cent showed abnormal adaptation in the winter and 5 per cent in the fall. Of 54 adults studied in Tennessee [55] 27 had subnormal abilities to adapt to darkness. In Copenhagen [56] 46 of 65 healthy school children showed this impairment. Similar findings have been reported from France,[57] Sweden,[58] Finland,[59] Germany,[60] India,[61] Africa [29] and the Dutch East Indies.[62] However, reports indicating a very low incidence of dark dysadaptation are also available. A study of Chicago children [63] in 1942, augmented by determinations of vitamin A blood levels, led to the conclusion that "mild vitamin A deficiency is rare or not detectable by these methods." Only 1 case of dark dysadaptation [64] was found among 144 New York City school children.

Very mild degrees of conjunctival xerosis recently have been attributed to a deficiency of vitamin A. By means of a bimicroscopic slit lamp, 86.6 per cent [6] of poor school children in New York City were found to exhibit such lesions. A follicular conjunctivitis also

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63. Oldham, Helen; Roberts, Lydia J.; MacLennan, Kathryn, and Schlutz, F. W.: J. Pediat. **90:** 740 (June) 1942.
64. Lewis, J. M., and Haig, C.: J. Pediat. **16:** 285 (March) 1940.

thought to be etiologically related to vitamin A deficiency was present in 21.7 per cent of 1,041 Florida [65] school children.

VITAMIN D DEFICIENCY

Nutritional diseases due to deficiencies of vitamin D and calcium may be divided into three important categories, namely rickets, osteomalacia and tetany. The three conditions, though usually separated for descriptive purposes, have ramifications that make it difficult to separate them completely.

Rickets.—Neff [66] defines rickets as a "nutritional and metabolic disease of the first two years of life, the chief characteristic of which is a failure to appropriate or retain calcium in the bones, which become soft and deformed."

The existence of rickets has been demonstrated throughout most of the world, varying in its frequency and severity in various localities. The greatest local prevalences were found in larger cities where poor housing, inadequate diets and limited exposure to sunshine exists. The disease has been reported to be, as a rule, most prevalent in the north temperate zone and least prevalent in the tropical and subtropical areas.

An incidence of 75 to 97.6 per cent of children having symptoms of rickets has been reported in certain areas of the United States,[67] in Germany,[68] Italy,[69] Sweden,[70] the British Isles [71] and Egypt,[72] in from 25 to 75 per cent of children in Switzerland,[73] in the United States,[74] the British Isles [71] and Argentina,[75] among nomad Laplanders,[76] in the cantons of Colmar and Andolscheim,[77] in Norway [78] and Germany [79] and from 0 to

TABLE 3.—*Occurrence of Rickets*

Area Reported	Year	Number Examined	Number or Percentage of Cases Found	References
Incidence of 75 to 97.6%				
Portland, Ore.	1936	1,000	97.6%	Moore and Dennis [69]
Hamburg, Germany	....	....	95 %	
Riga	....	....	86 %	
Boston	....	....	79 %	
Dresden, Germany	....	....	89 %	
Durham, England	1935	1,287 boys	81.8%	McIntosh [71]
Durham, England	1935	1,122 girls	76 %	
Lund, Sweden	1934	141	108 or 76 %	Siwe [70]
Portland, Ore., and San Diego, Calif.	1937	913	90 %	Moore and others [67]
	About equal number in each city			
Frankfurt, Germany	1939	599	80.8%	Graser [68]
Reich, Germany	Winter of 1940	....	75 %	Rott [68]
Germany	Winter of 1939	599	75 %	Graser [68]
Incidence of 25 to 74.9%				
Egypt	1935	....	50 %	Sabri [72]
Egypt	1938	240	104 or 43.3%	Huldschinsky [72]
Lausanne, Switzerland	1937	438	271 or 64.3%	Messerli [73]
Kings Lynn, England	1935	651 boys	29.1%	McIntosh [71]
Buenos Aires, Argentina	1932	1,000	356 or 35.6%	Sujoy [75]
Buenos Aires, Argentina	1934	408	32 %	Garrahan [75]
Buenos Aires, Argentina	1939	186	36.8%	Giordano [75]
Nomad Laplanders	1939	140	44 or 31.4%	Gezelium [76]
Cantons of Colmar and Andolschein	1936	192	45 %	Zillhardt [77]
Baltimore	1943	230	46.5%	Follis, Jackson, Eliot and Park [74]
Norway (inland)	Not given	917	Under 1 yr. 30 % 1 to 3 yrs. 40 %	Rustung [78]
City of Freiberg, Germany	1936	1,431	47 %	Viethen [79]
Adjoining rural districts	1936	....	70 %	
Sudetenland	1940	....	30 to 70 %	Hofmeier [79]
Reich, Germany	Summer of 1940	....	50 %	Rott [68]
Germany	June and July 1941	412	42 %	Graser [68]
Aussig, Germany	1938-1939	4,439	2,918 or 65.7%	Reichsgsndtsbl. **14**: 343, 1942
Incidence of 0 to 24.9%				
Hong Kong, China	1939	....	None	Wellington [80]
Panama Canal Zone	1933	100	8 or 8 %	Elliot and Jackson [81]
Puerto Rico	1933	564	5 or 0.9%	
Palestine	1937	950 sick children in hospitals	11 or 1.1%	Gruenfelder [82]
Palestine	1937	6,203 outpatients	57 or 0.9%	Gruenfelder [82]
Uruguay	1937	Children hospitalized in early infancy	15 to 12 %	Carran and Bazzano [83]
Africa	1939	2,000	4 or 0.2%	Niosi [84]
France	1936	In schools in cities and villages	4 to 6 %	Freyss [85]
Haiti	1936	....	Relatively rare	Armand, M.: Gaz. méd. Paris **43**: 53, 1936
Swedish Laplanders	1936	....	Practically no rickets	Schwenk, E.: München. med. Wchnschr. **83**: 1395, 1936
Hamburg, Germany	1929	668	101 or 15.1%	Zell, W., ibid. **84**: 1895, 1937
Hamburg, Germany	1936	1,245	21.2%	
Italy	1938	....	0.5 to 1.5%	Petragnane [86]
Ecuador	1936	....	Rickets in exceptional cases	Velasco [87]
Haiti	1936	....	Relatively rare	Armand [88]
Honduras	1936	....	Very rare	Ordonezdiaz [89]
Peru	1933	32,000	0.18%	Suares [90]
Peru	1934	32,000	0.16%	

65. Sandels, Margaret R.; Cate, Helen D.; Wilkinson, Kathleen P., and Graves, L. J.: Follicular Conjunctivitis in School Children as an Expression of Vitamin A Deficiency, Amer. J. Dis. Child. **62**: 101 (July) 1941.

66. Neff, Frank C.: Rickets, in Tice's Practice of Medicine, **9**, Sec. XIII, chapter VIII, Hagerstown, Md., W. F. Prior Company.

67. Moore, C. U.; Brodie, Jessie L.; Thornton, A. J.; Lesem, A. M., and Cordua, Olive B.: Failure of Abundant Sunshine to Protect Against Rickets, Am. J. Dis. Child. **54**: 1227 (Dec.) 1937. Moore and Dennis.[69]

68. Graser, E.: Ztschr. f. Kinderh. **61**: 520, 1939. Rott, H. J.: Reichsgesdbl., 1940. Graser, E.: Klin. Wchnschr. **21**: 82, 1942. Moore and Dennis.[69]

69. Moore, C. U., and Dennis, H. G.: California & West. Med. **44**: 288 (April) 1936.

70. Siwe, S.: Acta pædiat. **17**: 1, 157, 184, 1934.

71. McIntosh, J. W.: J. State Med. **43**: 187 (April) 1935.

72. Huldschinsky, K.: Brit. J. Phys. Med. **1**: 297 (Sept.) 1938. Sabri, S.: J. Egyptian M. A. **18**: 138 (Feb.) 1935.

73. Messerli, F. M.: Rev. d'hyg. **59**: 640, 1937.

74. Follis, R. H., Jr.; Jackson, Deborah; Eliot, Martha M., and Park, E. A.: Prevalence of Rickets in Children Between Two and Fourteen Years of Age, Am. J. Dis. Child. **66**: 1 (July) 1943.

75. Sujoy, E.: Semana méd. **40**: 646, 1933. Garrahan, J. P., and Muzio, E., ibid. **41**: 392, 1934. Giordano, J. J., ibid. **46**: 460, 1939.

76. Gezelium, G.: Acta pædiat. **26**: 184, 1939.

77. Zillhardt, A.: Bull. Soc. pediat., Paris **34**: 373, 1936.

78. Rustung, E.: Acta pædiat., 1935, **17**, supp. 2, p. 33.

79. Viethen, A.: Arch. f. Kinderh. **115**: 13, 1938. Hofmeier, K.: ibid. **120**: 49, 1940. Zell, W.: München. med. Wchnschr. **84**: 1895, 1937. Rott.[68] Graser.[68]

25 per cent in localities in China,[80] the Panama Canal Zone,[81] Puerto Rico,[81] Palestine,[82] Uruguay,[83] Africa,[84] France,[85] Italy,[86] Ecuador,[87] Haiti,[88] Honduras [89] and in Peru.[90]

The disease in itself is rarely fatal, but intercurrent infections may develop that are difficult to control, owing to the low resistance of the individual. The Bureau of the Census [91] for the United States lists rickets as a cause of death in each of nine years from 1933 through 1941 as ranging from 339 to 139. In England and Wales [92] it was listed as the cause of death for eleven years from 1928 through 1938 as ranging from 493 to 124. There were 554 deaths in Italy in 1937,[93] 129 in Colombo, Ceylon, in 1939,[94] 21 deaths of 57 patients with rickets admitted to all hospitals in the Malaya States in 1938 [95] and 170 deaths of 195 patients with rickets in hospitals in Chile in 1942.[96]

Osteomalacia.—This is a nutritional disease of adults resulting from deficiency of vitamin D and the failure of utilization of calcium. It is characterized by pro-

TABLE 4.—*Deaths from Rickets*

Area Reported	Year	Number of Deaths	References
United States	1933	339	U. S. Bureau of the Census [91]
	1934	292	
	1935	261	
	1936	270	
	1937	235	
	1938	244	
	1939	143	
	1940	161	
	1941	139	
England and Wales	1928	493	Register General Statistical Review of England and Wales for 1938 [92]
	1929	416	
	1930	316	
	1931	461	
	1932	301	
	1933	213	
	1934	180	
	1935	159	
	1936	148	
	1937	158	
	1938	124	
Italy	1937	554	Statistica, 1937 [93]
Malaya States	1939	129	de Pinto [94]
Colombo, Ceylon	1938	21 of 57 hospitalized	Straits Settlements report [95]
Chile	1942	170 of 195 hospitalized	Alimentacion in Chile [96]

nounced softening of bones, so much so that they become flexible and cause deformities, especially of the limbs, spine, thorax and pelvis. It is attended by the rheumatic type of pain and general weakness. Although it is occasionally seen in men it is most often encountered in women, especially among those who are pregnant.

Although osteomalacia has become an exceptional disorder among peoples living under modern civilizations, there are still large areas where it constitutes a medical problem. It was reported to be widely distributed in India,[97] in the province of Shansi, China,[98] in the province of Toyama, Japan,[99] and in an isolated district of Bosnia,[100] where 3,510 cases were seen in the twelve years previous to 1910. The disease is most frequently found in India among women of the upper and middle classes who practice seclusion or purdah after marriage. It is seldom found among the lower classes who have to work outdoors.

This disease and rickets have the same etiologic factors, viz. vitamin D deficiency and disturbance of calcium metabolism; also no sharp distinction can be drawn between late or adult rickets and osteomalacia. It has been reported [101] that among 1,000 children of well-to-do parents whose mothers observe purdah 25 per cent had rickets, whereas among 2,300 children of low caste Hindus only about 5 per cent were affected.

"War Osteopathy," or "Hunger Osteomalacia."—A nutritional disorder which was generally termed "war osteopathy" or "hunger osteomalacia" made its appearance among the peoples of central Europe shortly after World War I. It was common in Austria, Germany and Poland. This disorder was characterized by pains in the back, groins and legs, by a somewhat characteristic gait, by difficulty in climbing stairs and by some tenderness of the bones. The age and sex distribution was peculiar. Beninde [102] stated that there was pronounced susceptibility of adolescents, mainly males; almost no cases occurred between the ages of 20 and 35, whereas the high incidence was in the period from 40 to 60 years, confined almost entirely to women. Hess [103] states that the condition "developed to a degree and extent such as had never been experienced in the history of medicine. Marked deformities of the spine and the extremities, multiple fractures, and functional disabilities by the thousand, were observed throughout the land." He reasons that from the very close resemblance between this condition and the classic osteomalacia it would seem of advantage to class them as one and the same disorder.

Tetany.—This is a syndrome manifested by sharp flexion of the wrists and ankle joints, muscle twitchings, cramps and convulsions. It is due to abnormal calcium and phosphorus metabolism. It may be associated with several conditions, but consideration here is given only to its association with vitamin D deficiency in relation to rickets and osteomalacia. As in rickets, the peak of the incidence of tetany is in late winter and early spring.[104]

Tetany has often been noted in cases of rickets and osteomalacia. In one report [105] it was recorded that one fifth of the cases of rickets and one third of their cases of osteomalacia showed signs of tetany. In another report [106] it was stated that 30 of 63 patients with

80. Wellington, A. R.: Hong Kong M. & San. Report for Year 1932, p. 60.
81. Elliot, Martha M., and Jackson, Edith B.: Bone Development of Infants and Young Children in Puerto Rico, Am. J. Dis. Child. **46:** 1237 (Dec.) 1933.
82. Gruenfelder, B.: M. Rec. **146:** 176, 1937.
83. Carran, A., and Bazzano, H. C.: Arch. pediat. Uruguay **8:** 428, 1937.
84. Niosi, A.: Minerva Med. **30:** 454, 1939.
85. Freyss, M. M.: Bull. Soc. pediat., Paris **34:** 374, 1936.
86. Petragnane, G.: Bul. Off. internat. hyg. **30:** 2257, 1938.
87. Velasco, C.: Bol. Inst. Intern. Am. Prolec. Infan. **9:** 3, 1936.
88. Armand, M.: Bol. Inst. Intern. Am. Prolec. Infan. **9:** 3, 1936.
89. Ordonezdiaz, P. H.: Bol. Inst. Intern. Am. Prolec. Infan. **9:** 3, 1936.
90. Suares, L. A.: Bol. Inst. Intern. Am. Prolec. Infan. **9:** 3, 1936.
91. Bureau of the Census of the United States.
92. The Register General Statistical Review of England and Wales for the year 1938.
93. Statistica de il cause di morte, 1937.
94. de Pinto, C. E.: Report on Vital Statistics, 1939.
95. Ann. Report of Medical Dept. Sts. Settlements Federated Malay States and Unfederated Malay States, 1938.
96. La Alimentacion, in Chile, 1942, p. 260.
97. Scott, A. C.: Indian J. M. Res. **4:** 140, 1916.
98. Maxwell, J. P.: China M. J. **37:** 625, 1923.
99. Ogata, M.: Beitrage z. Geburtsh. u. Gynäk. **17:** 23, 1911; **18:** 8, 1912.
100. Januszewska, G.: Wien. klin. therap. Wchnschr. **17:** 503, 1910.
101. Huchison, H. S., and Shah, S. J.: Quart. J. Med. **15:** 167, 1922.
102. Beninde, M.: Ver. a. d. Geb. d. Medizinalverwaltung **10:** 1, 1920.
103. Hess, A. F.: Rickets, Osteomalacia and Tetany, Philadelphia, Lea & Febiger, 1929.
104. Kassowitz, M.: Praktische Kinderheilkunde, Berlin, Springer, 1910. Frankl-Hochwart, L.: Die Tetanie der Erwachsenen, Vienna, Haetder, 1907. Japha, A.: Arch. f. Kinderh. **42:** 66, 1905.
105. Huchison, H. S., and Stapleton, G.: Brit. J. Dis. Child. **21:** 18, 1924.
106. Stapleton, G.: Lancet **1:** 1119, 1925.

rickets had tetany, while in another [100] it was noted that tetany occurred in 338 of 3,510 cases of osteomalacia seen in Bosnia.

Tetany in rickets may be the immediate cause of death. This comes about either by the result of heart failure following spastic contraction of the heart muscle or by respiratory failure of cerebral origin. Happily this result is infrequent, as there are many therapeutic measures available for rapidly controlling the convulsive seizures. Some cases, however, resist all measures.

Reports in recent years on incidence of tetany in various localities are limited as a rule to individual case reports. Snelling and Brown [107] reported 32 cases in 1928 and 28 in 1935 at the Hospital for Sick Children in Toronto, Canada. Hennig [108] observed 79 cases of manifest tetany in central Europe from 1933 to 1937.

(To be continued)

Council on Pharmacy and Chemistry

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING STATEMENT. AUSTIN E. SMITH, M.D., Secretary.

THE USE OF VITAMIN D IN THE TREATMENT OF REFRACTORY RICKETS

The Council has given consideration to the use of relatively massive doses of vitamin D in the treatment of refractory rickets and has accepted at least one preparation designed for such use. As a result of this consideration and acceptance the Council has voted to revise the statement on vitamin D (New and Nonofficial Remedies, 1943, pages 582-583) by the addition of the following paragraph:

Another suggested use of massive doses of vitamin D is in the treatment of refractory rickets, that is, occasional cases of rickets which do not respond to treatment with the usual dosages or even much larger dosages of vitamin D. In some of these cases the rickets is due to a disturbance of the acid base balance and has been successfully treated by administration of sodium bicarbonate or a sodium citrate-citric acid mixture. Massive doses of vitamin D have proved effective in the control in others. The quantity of vitamin D needed may be so large that it borders on the dosages of vitamin D that are definitely toxic, and such treatment should not be undertaken without first exploring other possibilities or without careful observation for signs of toxicity. Some investigators believe it desirable to examine the urine daily for calcium casts, albumin and red blood cells while the maintenance dose is being established. Others believe less frequent examination is necessary. After the dose is established weekly examination, using the Sulkowitch test for excessive excretion of calcium, is sufficient. The blood should be examined weekly or oftener to avoid a rise of calcium above 12 mg. per hundred cubic centimeters if the dosage exceeds 20,000 units daily for the infant or 50,000 units for a child. If anorexia or nausea should appear, the child must be brought promptly to the attention of the physician and vitamin D administration should be discontinued. When the maintenance dose has been established, operative procedures to correct rachitic deformities may precipitate a temporary state of toxicity and the blood levels of calcium must be watched closely.

The Council voted further to revise the "Allowable Claims" which appear on pages 583-584 by the addition of the following sentence to claim 6, which appears on page 584:

If representations are made for use of massive doses of vitamin D in the treatment of refractory rickets they must be accompanied by adequate precautions with respect to the danger of toxic effects and how they can be avoided.

107. Snelling, C. E., and Brown, Alan: J. Pediat. **10**: 167 (Feb.) 1937.
108. Hennig, E.: Ztschr. f. Kinderh. **61**: 379, 1939.

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

AUSTIN E. SMITH, M.D., Secretary.

VITAMIN B COMPLEX PREPARATIONS (See New and Nonofficial Remedies, 1943, p. 588).

The following products have been accepted:

ABBOTT LABORATORIES, NORTH CHICAGO, ILL.

Brewers' Yeast Powder Fortified with Riboflavin and Nicotinic Acid: Contains dried brewers' yeast (Saccharomyces cerevisiae), debitterized, fortified with crystalline riboflavin and nicotinic acid to contain in each gram vitamin B_1 50 U. S. P. units (0.15 mg.), riboflavin 0.3 mg. and nicotinic acid 1.5 mg. Daily prophylactic dose for infants, ½ level teaspoon; children 1 to 6 years old, 1 level teaspoon; children 6 to 12 years old, 1½ level teaspoons; older children and adults, 2 level teaspoons mixed with water, milk or fruit juices.

Brewers' Yeast Tablets, 0.4 Gm. (6 grains), Fortified with Riboflavin and Nicotinic Acid: Each tablet contains Abbott's Brewers' Yeast Powder Fortified with Riboflavin and Nicotinic Acid 0.4 Gm., providing in each tablet vitamin B_1 20 U. S. P. units (0.06 mg.), riboflavin 0.12 mg., nicotinic acid 0.6 mg. Average daily dose, as a supplement to the diet, for children 6 to 12 years old, 6 tablets; older children and adults, 9 tablets; therapeutic doses must be determined for each patient.

DIGITALIS (See New and Nonofficial Remedies, 1943, p. 289).

The following dosage forms have been accepted:

PITMAN-MOORE COMPANY, INDIANAPOLIS

Tablets Digitalis: 32 mg. (½ grain) (⅓ U. S. P. unit); 65 mg. (1 grain) (⅔ U. S. P. unit) and 0.1 Gm. (1½ grains) (1 U. S. P. unit) (keratin coated).

Pulvo-Caps Digitalis: 0.1 Gm. (1½ grains) (1 U. S. P. unit) and 65 mg. (1 grain) (⅔ U. S. P. unit).

Tincture Digitalis: Four fluidounces and 1 pint bottles.

OLEOVITAMIN A (See New and Nonofficial Remedies, 1943, p. 587).

The following dosage form has been accepted:

INTERNATIONAL VITAMIN SALES CORP., NEW YORK

Oleo Vitamin A Capsules: Each capsule contains 25,000 U. S. P. units of vitamin A derived from fish liver oils.

PROCAINE HYDROCHLORIDE (See New and Nonofficial Remedies, 1943, p. 82).

The following dosage forms have been accepted:

E. S. MILLER LABORATORIES, INC., LOS ANGELES

Sterile Solution Procaine Hydrochloride 1% W/V: 30 cc., 50 cc. and 100 cc. vials and 2 cc. and 5 cc. ampuls. Preserved with 0.5 per cent chlorobutanol.

Sterile Solution Procaine Hydrochloride 2% W/V: 30 cc., 50 cc. and 100 cc. vials and 2 cc. and 5 cc. ampuls. Preserved with 0.5 per cent chlorobutanol.

RABIES VACCINE CHLOROFORM KILLED (See New and Nonofficial Remedies, 1943, p. 543).

The following dosage form has been accepted:

THE GILLILAND LABORATORIES, INC., MARIETTA, PA.

Rabies Vaccine (Chloroform Killed Virus): 0.5 cc. vials packaged in units of seven and fourteen vials.

SULFADIAZINE (See New and Nonofficial Remedies, 1943, p. 169).

The following dosage forms have been accepted:

E. R. SQUIBB & SONS, NEW YORK

Tablets Sulfadiazine: 0.5 Gm.

Sulfadiazine Powder (Sterilized): 5 Gm. vial.

SULFADIAZINE SODIUM (See New and Nonofficial Remedies, 1943, p. 188).

The following dosage forms have been accepted:

E. R. SQUIBB & SONS, NEW YORK

Sulfadiazine Sodium Powder (Sterilized): 5 Gm. vial.

Sulfadiazine Sodium Powder (Nonsterilized): 50 Gm. bottle.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, OCTOBER 2, 1943

INFLUENZA RECEPTOLYSIN

New facts regarding the mechanism of virus infections of the respiratory epithelium have resulted from studies of virus hemagglutinins recently reported by Hirst [1] of the International Health Division, Rockefeller Foundation. Two years ago Hirst noted that influenza virus grown in the allantoic fluid of chick embryos would agglutinate adult fowl erythrocytes. This hemagglutinin could be used as a reliable quantitative index of the mouse infectious titer of influenza virus and for the titration of anti-influenza serums. The observation was promptly confirmed by other investigators,[2] who reported evidence that the influenza virus is actually adsorbed on fowl erythrocytes, from which it can be partially or wholly recovered by elution.

Quantitative studies of the rate and completeness of this virus adsorption yielded surprising results. For example, Hirst found that addition of the Lee strain of influenza B virus to a 1.5 per cent suspension of chicken erythrocytes caused the titer of the free, or uncombined, virus to fall from 128 units to less than 4 units by the end of ten minutes, a 94 per cent adsorption of the virus on the red blood corpuscles. This adsorption, however, did not result in a permanent chemical union between virus and erythrocytes; release of the adsorbed virus was noted within twenty minutes, increasing to a measurable amount by the end of two hours. There was no demonstrable multiplication of the virus in the blood suspension to account for this release.

The released virus was apparently unaltered as a result of its previous adsorption on the erythrocytes. The blood cells, however, were definitely changed, as shown by their acquired insusceptibility to subsequent agglutination with influenza virus. To account for this insusceptibility, Hirst postulated the existence of specific haptens or receptor materials on the fowl erythrocytes, which he had reason to believe were complex polysaccharides. He assumed further that this receptor substance is destroyed by enzymes (or functions) of the influenza virus. Release of the virus was therefore pictured as a result of receptor hydrolysis, the resulting dehaptenized erythrocytes being incapable of adsorbing influenza virus. This is essentially a renaissance of the original Pasteur exhaustion theory of acquired immunity.

It seemed likely to Hirst [3] that this in vitro adsorption and release of influenza virus might have its counterpart in the reactions between influenza virus and respiratory epithelium. He therefore repeated the experiments using mouse, rabbit and ferret lungs in place of fowl erythrocytes. The lungs were first perfused free from blood and then suspended in an Erlenmeyer flask with a side arm by means of which the external pressure could be increased or decreased. Virus infected allantoic fluid was introduced into the trachea of the suspended lungs, and the lungs were alternately expanded and compressed to insure uniform mixture. Samples of the allantoic fluid were removed at intervals and titrated for hemagglutinins and for their lethal effects on mice. These titrations showed an extremely rapid adsorption of the virus on the respiratory epithelium. With the PR8 virus less than 1 per cent remained unabsorbed after five minutes of the simulated respiratory movements. This was followed by a fairly rapid release of the virus, the original titer of the allantoic fluid being restored almost quantitatively in from two to five hours. As in previous tests with red blood cells, the rapidity of the adsorption and subsequent release of the virus varied with different viral strains. Heat inactivated and formaldehyde inactivated influenza viruses were also adsorbed and at the same rate, but there was no evidence of their subsequent release, presumably owing to inactivation of their enzymic function.

In order to test possible clinical applications of these observations, the tests were repeated on the intact lungs of living ferrets. In the case of ferrets killed at stated intervals after intratracheal inoculation, adsorption of the virus had taken place in the viable lung in much the same way as in the isolated blood free lungs. The adsorbed virus, however, remains permanently adsorbed on the epithelial cells of the living lungs,

1. Hirst, G. K.: The Agglutination of Red Cells by Allantoic Fluid of Chick Embryos Infected with Influenza Virus, Science **94**: 22 (July 4) 1941; The Quantitative Determination of Influenza Virus and Antibodies by Means of Red Cell Agglutination, J. Exper. Med. **75**: 49 (Jan.) 1942; Adsorption of Influenza Hemagglutinins and Virus by Red Blood Cells, ibid. **76**: 195 (Aug.) 1942.

2. McClelland, Laurella, and Hare, Ronald: The Adsorption of Influenza Virus by Red Cells and a New In Vitro Method of Measuring Antibodies for Influenza Virus, Canad. Pub. Health J. **32**: 530 (Oct.) 1941.

3. Hirst, G. K.: Adsorption of Influenza Virus on Cells of the Respiratory Tract, J. Exper. Med. **78**: 99 (Aug.) 1943.

release being still absent at the end of eight hours. A slight apparent release of one virus was noted at the end of twenty-four hours, presumably because of multiplication.

Assuming that virus release is due to enzymic hydrolysis of the specific receptor substance, one might be tempted to postulate that this nonrelease is due to enzyme inhibitors in the living tissue cells or adjacent blood plasma. Hirst, however, is inclined to attribute it to aggressive growth of the attached virus under natural conditions of infection, destruction of the specific receptor substance being a necessary preliminary to parasitism on or within susceptible tissue cells.

Aside from its theoretical interest, isolation and identification of the postulated specific receptor substance have numerous suggestive practical applications. Hirst's work, therefore, may well lead to new methods of influenza prophylaxis and therapy. The work is being continued in the International Health Laboratory.

THE INTERNATIONAL RED CROSS IN TIME OF WAR

The International Red Cross was born of war and still serves most actively in wartime. The International or Geneva Red Cross movement rests on the foundation of the individual national organizations even though these vary widely in structure and importance in different countries. Since 1928 the International Red Cross has been a three headed organization which includes the national societies of the Red Cross, the International Committee and the League of the Societies of the Red Cross.[1]

During the war of 1870 the International Committee assumed for the first time the assistance to prisoners of war and created an agency for prisoners at Basle. Later this agency was removed to Geneva. Past experiences were reviewed in 1929; this resulted in the adoption of the revised convention of Geneva in that year regarding the treatment of prisoners of war. This convention was ratified by most countries except Finland, Japan, Russia and certain countries of Latin America.

The principal features of this code relate to the visiting of camps for prisoners of war by delegates of the International Committee. The official delegates may consult with trusted prisoners ("hommes de confiance") who have been selected by their comrades and who represent them. These visits to camps make it possible for the delegates of the committee to request the camp authorities for improvements; they allow for the intervention of the International Committee itself. By reciprocity these visits permit equal improvements to be made in the conditions of prisoners of war held by the other side.

The Central Agency for Prisoners in Geneva is concerned not only with prisoners of war but with all categories of war victims including wounded and sick, civilian internees, military internees in neutral countries, refugees in their own countries and civilians separated from their families by hostilities. This agency is consequently a vast organization with four big buildings in Geneva and 3,500 workers; it has received over 19 million letters and telegrams and has dispatched some 20 million. Some 60 thousand letters are received by this agency each day.

Cards of notice of capture are worded by the prisoners themselves. The prisoners are permitted to send these cards to their families and at the same time to the central agency after they reach camp. The agency also carries through special inquiries for prisoners, notably when sick, or for those who have disappeared. These inquiries allow more complete information to be transmitted to the families. Another function of the International Committee is to arrange for the repatriation of the severely wounded. This ordinarily involves an exchange, usually through a neutral country. The interests of civilian internees and civilians in general are also represented by the International Committee. The committee collaborates with the diplomatic representatives of the powers, aids in problems of transportation, reports all violations of the conventions and is sometimes called on to enter into relations with governments, National Red Cross Societies or in unusual judicial situations.

A monthly journal in French records much of the current work of the International Red Cross. Of particular interest to Americans are the reports of visits to military prison camps and civilian internees in Japan proper and in such places as Shanghai and Hong Kong. Japan, although not a signatory of the Geneva Convention, previously indicated its intention of complying with its provisions. In most camps visited, conditions for both military personnel and civilians appear to be satisfactory. One recent report concerning the Stanley Camp for interned civilians at Hong Kong makes the somewhat enigmatic statement that the composition of rations has been recently improved. Reports on Japanese camps for Chinese and vice versa and on Russian camps for Axis prisoners and the reverse are missing.

Altogether the International Red Cross exerts a powerful force toward the amelioration of the effects of war and represents an extension of the endeavors of the medical profession throughout its long history.

1. Pictet, Jean S.: Revue Internationale de la Croix-Rouge, Geneva, February 1943.

Current Comment

WAR SURGERY IN THE MIDDLE EAST

During the last nine months of 1942, 3,279 battle casualties were admitted to one military hospital on the lines of communication in the Middle East. Because of the enemy's rapid advance to El Alamein the arrival of wounded was so rapid that the hospital had to act as a casualty clearing station rather than as a base hospital. The mortality rate for the 300 casualties from Tobruk was 3 per cent and for the 500 casualties from the second battle of El Alamein it was 10 per cent. The mortality rate for 2,679 casualties from the first battle of El Alamein, when the hospital acted as a casualty clearing station, was only 1.3 per cent. The high mortality rate for the casualties from Tobruk and from the second battle of El Alamein is due to the fact that seriously ill patients were sent to the hospital. The figure 1.3 per cent is approximately accurate for most casualty clearing stations. In analyzing the results, Lieut. Col. R. K. Debenham [1] emphasizes that all of the wounds dealt with were a result of fighting in dry sandy desert, that the amount of clothing worn was very small so that only rarely was clothing found in a wound, and that sulfanilamide was used prophylactically. As a routine 10 Gm. was dusted into the wound and another 10 Gm. after operation; 5 tablets (2.5 Gm.) were given by mouth at 6 a. m. and 6 p. m. daily for four days. The good results obtained in abdominal cases, particularly in those with bowel perforation, were due to early operation. Of the 11 patients with bowel perforation, the 9 who recovered were operated on in forward areas and were kept there from five to sixteen days; the cardinal points seem to be early operation, late evacuation, intravenous saline drip, continuous gastric suction and sulfadiazine. This is difficult with mobile warfare but was possible when the line of battle was static. The worst cases of burns came from fighting in tanks. Because facilities for preliminary cleansing were not obtainable, tanning was discarded in favor of cleansing and powdering the area with sulfanilamide and dressing with petrolatum gauze. Patients traveled best with plenty of padding, and for wounds of limbs a light, well padded plaster of paris cast was definitely beneficial. In the early stages intravenous plasma or serum was considered essential. Blood transfusions were used for secondary anemia a week or ten days later. Patients with severe burns traveled badly, even up to two weeks after burning. After a long journey they arrived toxic and ill. It is easy to put too much sulfanilamide powder on the burns, especially in severe cases, as sulfanilamide is readily absorbed from burned areas and gives rise to profound toxemia. Blood and plasma or serum transfusions were used for shock, for burns and during convalescence when the hemoglobin fell below 60 per cent. Gas gangrene has been rare and gas infection uncommon. No case of tetanus has been seen. Among the "don'ts" to be observed are listed:

Don't suture wounds. Don't suture amputation stumps.
Don't amputate at the site of election; go below it.
Don't use packing except to stop hemorrhage.
Don't use drainage tubing.
Don't use unpadded plasters.
Don't forget to give morphine before a long bumpy journey.
Don't forget to give plenty of fluids by mouth.
Dont forget that the ligature of a main vessel should be prominently recorded on the field medical card and underlined.

The salient features of war surgery in the Middle East are based on the principles which have been in the process of evolution since the beginning of the war. They are summarized as follows: organized resuscitation and the use of local and general sulfanilamide; thorough immobilization; conservative surgery and wound trimming instead of wound excision; avoidance of tension around wounds and provision of a good blood supply in damaged limbs, and the necessity to adapt and improvise articles to fulfil functions for which they were not intended.

1. Debenham, R. K.: War Surgery in the Middle East, Brit. M. J. 2: 223 (Aug. 21) 1943.

PERSONAL LIABILITY TO ACCIDENT

The toll from accidents in 1942 was 93,000 killed and 9,200,000 injured. According to the National Safety Council [1] two out of three industrial accidents—and many of the nonindustrial ones—have personal as well as mechanical causes. The importance of identifying accident-prone persons preferably before the occurrence of the accident is hence obvious. Dunbar [2] discusses a series of tests based on educational and vocational histories, family relations and information from personal observations, especially with regard to interests and addictions, attitude toward authority and impulsive behavior, by means of which it is believed that accident-prone persons can be identified with reasonable accuracy. The major sphere of difficulty of the accident-prone person appears to lie in the frequency of conflict with authority and the means by which such conflict is resolved. The tendency toward impulsive behavior, on which evidence may be gathered both from past history and from observation of actual behavior under stress, is also of importance, Dunbar says. If the validity of the proposed methods of selecting accident-prone persons can be confirmed—and ample opportunities are available to do so both in industry and in military life now—much may be learned concerning the possibilities for reeducation and the selection of persons for exclusion from certain occupations. Under the stress of war the available technics can be more readily evaluated just as the problem of accident prevention becomes even more than usually acute.

1. Accident Facts, 1943 Edition, National Safety Council, Inc., Chicago.
2. Dunbar, Flanders: Medical Aspects of Accidents and Mistakes in the Industrial Army and in the Armed Forces, War Med. 4: 161 (Aug.) 1943.

MEDICINE AND THE WAR

In this section of The Journal each week will appear official notices by the Committee on War Participation of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medicine and the war, and such other information and announcements as will be useful to the medical profession.

ARMY

EXAMINATION DATES FOR CANDIDATES FOR MEDICAL CORPS, REGULAR ARMY

The War Department announced on September 7 that examinations for the purpose of qualifying candidates for appointment as first lieutenants in the Medical Corps, Regular Army, to fill vacancies occurring during the fiscal year 1945 will be held on Jan. 24 through Jan. 27, 1944. The examinations are open to all male citizens of the United States who are graduates of acceptable medical schools in the United States and Canada, who have completed one year's internship in an approved hospital and who will not be over 32 years of age at the time it will be possible to tender a commission. The examinations will be conducted by boards of medical department officers and will consist of a physical examination, a written examination in professional subjects and a determination of the candidate's adaptability for military service. Candidates who fail a first examination will not be permitted to take more than one subsequent examination.

Full information and application blanks will be furnished on request by the Adjutant General, War Department, Washington 25, D. C. Applications from candidates in the continental limits of the United States received after Jan. 7, 1944 will not be considered.

TWENTY-FOURTH CLASS OF MEDICAL ADMINISTRATIVE CORPS OFFICERS

The twenty-fourth class of Medical Administrative Corps Officers at the Officer Candidate School, Camp Barkeley, Texas, graduated on September 16. This class was the last to graduate under the twelve week training schedule. Future classes will complete a sixteen week program, which does not include any more material but emphasizes the physical aspects of training with more field exercises and bivouacs. The graduation address was delivered by Brig. Gen. Roy. C. Heflebower, school commandant, and the oath of office was administered by Major Miles G. Ball, M. A. C., executive officer.

ENLISTED WACS OFFERED OPPORTUNITY TO BECOME PHYSICAL THERAPY AIDES

The War Department announced on September 13 that qualified enlisted members of the Women's Army Corps will be given an opportunity to become physical therapy aides, with the relative rank of second lieutenant, serving in the Medical Department of the Army of the United States. The training courses in physical therapy will begin in October under the direction of the Surgeon General, who will select the WAC personnel to be trained. On successful completion of the study and three months' practice, the Wacs will be discharged from the Women's Army Corps and will be appointed as physical therapy aides. To be eligible for this course, applicants must be under 44 years of age, must have completed the WAC basic training and must have a degree in physical education or two years of college study emphasizing the biologic sciences. Successful applicants will receive six months of training in physical therapy in classes at universities and hospitals. On completion of those studies they will be assigned to selected army hospitals for practical experience in the treatment of wounded soldiers. The first groups selected will be sent to Leland Stanford University at Palo Alto, Calif., the University of Wisconsin at Madison, and the D. T. Watson School of Physical Therapy at the University of Pittsburgh. They will be trained at government expense and be quartered on or near the university campuses. Later it is expected that Walter Reed General Hospital, Washington, D. C., and other army general hospitals will participate in the training. Major Emma E. Vogel is the director of physical therapy aides.

MICHAEL REESE HOSPITAL UNIT IN ITALY

An army evacuation hospital built around the original Michael Reese Hospital Unit which was formed in Chicago is reported to have landed in Italy with the American Fifth Army. The hospital was immediately set up and can handle 1,000 patients and treat every type of casualty. Hundreds of tons of equipment were landed with the unit, and the personnel includes specialists in every branch of surgery. Lieut. Col. Philip A. Daly of Chicago is in command of the unit, and other medical personnel are as follows:

Major Alfred E. Jones, Chicago.
Major Manuel E. Lichtenstein, Chicago.
Major Samuel Perlman, Chicago.
Major Laurence M. Weinberger, Chicago.
Capt. Harry E. Barnett, Chicago.
Capt. Richard M. Bendix, Chicago.
Capt. David Z. Berger, Chicago.
Capt. Ernest D. Bloomenthal, Chicago.
Capt. Joseph A. Carbone, Gary, Ind.
Capt. Melvin R. Cohen, Chicago.
Capt. Norman R. Cooperman, Chicago.
Capt. Sol Ralph Friedlander, Chicago.
Capt. Richard E. Heller, Chicago.
Capt. Harold Laufman, Chicago.
Capt. Saul A. Mackler, Chicago.
Capt. Philip M. Marcus, Chicago.
Capt. William H. Parker, Oak Park, Ill.
Capt. Alfred J. Platt, Chicago.
Capt. Arthur H. Schoenwetter.
Capt. Morris J. Shapiro, Chicago.
Lieut. Sol Z. Draznin, Chicago.
Lieut. Samuel H. Fraerman,
Lieut. Jesse G. Garber, Chicago.
Lieut. Wilburt Gordon, Chicago.
Lieut. Ralph R. Landes, Chicago.
Lieut. Samuel M. Marcus, Chicago.
Lieut. Manuel L. Stillerman, Chicago.
Lieut. Leonard A. Stine, Chicago.
Lieut. Leonard Weinstein. Chicago.

DR. MEYER AWARDED SILVER STAR

Capt. Alfred C. Meyer, Chicago, of the Army Medical Corps has been awarded the Silver Star for heroism and outstanding achievement in operating on wounded soldiers while under Japanese gunfire in New Guinea. He is said to be serving with the first portable hospital to be established by the Army. A portable hospital is understood to be one in which the medical equipment and supplies are so packed and arranged that in jungle warfare they may be carried forward near the front lines, if necessary, by hand.

PRISONER OF THE JAPANESE

The first direct word from Capt. Gerald M. Greenspahn, formerly of Chicago, since Nov. 27, 1941 was recently received by his family, indicating that he is being held as a prisoner of the Japanese in the Philippines in prison No. 1. Captain Greenspahn graduated from Northwestern University Medical School, Chicago, in 1935 and was staff physician of the American Hospital before entering the service.

FLIGHT SURGEON'S ASSISTANTS

A class of ninety-nine flight surgeon's assistants completed the six weeks course in aviation medicine at the School of Aviation Medicine, Randolph Field, Texas, August 21. Brig. Gen. Eugen G. Reinartz, U. S. Army, is commandant of the school.

NAVY

COMMISSIONING OF APPRENTICE SEAMEN IN MEDICAL SCHOOLS ON COMPLETION OF MEDICAL EDUCATION

The Bureau of Naval Personnel of the Navy Department, Washington, D. C., has announced that apprentice seamen, Class V-12(S), who are medical students will, on satisfactory completion of their medical education, be appointed to the rank of Lieutenant (jg), (MC), U. S. Navy, or Lieutenant (jg), MC-V(G), U. S. Naval Reserve, in accordance with the following procedures:

(*a*) For appointment in the grade of Acting Assistant Surgeon, rank of Lieutenant (junior grade), (MC), U. S. Navy:

1. Students, within three months of completion of their junior year and at any time thereafter, may submit application to the Bureau of Medicine and Surgery via the commanding officer for examination for appointment as Acting Assistant Surgeon for intern training in the U. S. Navy. Commanding officers of Navy V-12 units at medical schools have been provided with a supply of the appropriate application forms.

2. The Bureau of Naval Personnel, on the recommendation of the Bureau of Medicine and Surgery, will authorize qualified applicants to participate in examinations which will be conducted at all continental U. S. naval hospitals during January, May and September of each year.

3. Candidates will receive official notification via their commanding officer of the results of their examination approximately two months following the date thereof.

(*b*) For appointment as Lieutenant (junior grade), MC-V(G), U. S. Naval Reserve:

1. Students who did not apply or failed to qualify on examination for a naval internship and have contracted for a civilian internship in lieu thereof will be eligible for this appointment on satisfactory completion of their medical education.

(*c*) Commanding officers of Navy V-12 units at medical schools are requested to submit to the Bureau of Naval Personnel via the Bureau of Medicine and Surgery sixty days prior to established graduation dates two lists in triplicate of senior class V-12(S) medical students under their command who have been reported by medical school deans as scheduled to graduate. One list should include only the names of those students who have qualified for appointment as Acting Assistant Surgeon for intern training in the U. S. Navy and the second list the names of those students committed to a civilian internship and thus qualified for appointment as Lieutenant (jg), MC-V(G), U. S. Naval Reserve. It is desired that there be incorporated in these reports data constituting the commanding officer's recommendation as to the possession of requisite officer-like qualities in each case together with remarks on the following points:

1. Whether any student who participated in an examination for appointment as Acting Assistant Surgeon has failed to receive official notification as to the results of his examination.

2. Whether each student who has qualified for appointment as Acting Assistant Surgeon intends to accept the appointment on graduation or to decline for the purpose of attending a civilian internship. In the latter case, graduates will be appointed Lieutenant (jg), MC-V(G), U. S. Naval Reserve, and released to an inactive duty status.

3. The names and locations of the hospitals in which Naval Reserve appointees will serve civilian internships indicating the type and duration (dates of commencement and completion) of the internship contracted for in each case.

4. The necessary delay, not to exceed thirty days, in reporting at the initial permanent duty station required by each individual for the purpose of taking state board medical examinations. (In cases in which state board medical examinations will not be completed during the thirty day period following graduation, newly appointed officers will report to assigned stations of duty and, at the appropriate time after reporting, submit a request to the commanding officer of the station to which assigned for such leave as may be necessary to participate.)

Commanding officers of V-12 units at medical schools where graduation dates have been established for October 1943 will forward the lists requested as soon as possible.

(*d*) The commanding officers are directed to forward a completed report of physical examination, form Y, in duplicate for each student named in the foregoing lists who is recommended for appointment.

(*e*) On receipt of this report from commanding officers, the Bureau of Medicine and Surgery will make appropriate recommendation by endorsement to the Bureau of Naval Personnel. Appointments will be issued for fully qualified applicants and will be forwarded to commanding officers for delivery on graduation.

(*f*) Appointments in the grade of Acting Assistant Surgeon for internship with the rank of Lieutenant (junior grade), (MC), U. S. Navy, will be accompanied in each case by active duty orders to the naval hospital to which such appointees have been assigned for intern training.

(*g*) Appointments as Lieutenant (junior grade), (MC-V(G), U. S. Naval Reserve, will be written with date of rank approximately ten days after graduation. If appropriate, commanding officers will furnish a transportation request and meal tickets covering return of these men as Apprentice Seamen, class V-12(S) or SV-12(S) to the place to which initial orders to active duty were addressed or they will be granted a travel allowance of 5 cents a mile in lieu thereof in accordance with the provisions of reference (*a*). These men will be instructed by the commanding officer to appear before a naval officer qualified to administer oaths or before a notary public on the date specified as "date of rank" in order to execute the acceptance and oath of office. The commanding officer shall explain clearly that a man cannot execute an acceptance and oath of office as a naval officer and subsequently use transportation forwarded to him as an enlisted man.

(*h*) The appointment for any man who fails to graduate will be returned by the commanding officer to the Bureau of Naval Personnel for cancellation and appropriate disposition of the man.

(*i*) Additional information relative to this subject will be found in references (*b*) and (*c*).

FOREIGN LANGUAGE REQUIREMENTS FOR PREMEDICAL STUDENTS

The Bureau of Naval Personnel of the Navy Department, Washington, D. C., announced on September 9 the interpretation of the foreign language requirements for premedical students as referred to in References (a) V-12 Bulletin No. 1, (b) V-12 Bulletin No. 22, and (c) V-12 Bulletin No. 2.

1. Reference (b), page 12c, language requirement for subject students shall be interpreted as follows:

V-1 and V-7 transfers to V-12, who are pursuing a premedical program, shall complete the equivalent of twelve college semester hours of a single foreign language. French, German or Spanish is preferred, but other languages may be substituted at the discretion of the college authorities. A high school unit (one year) is to be considered equivalent to six semester hours.

2. In accordance with reference (c), page 3, paragraph 8, other premedical students entering the V-12 program with advanced standing must meet minimal requirements prescribed for V-1 and V-7 transfers to V-12.

3. Only premedical students entering the V-12 program as freshmen will be required to take the fully prescribed course outlined in reference (a). Attention is invited to the fact that French, German or Spanish is preferred, but other languages may be substituted under exceptional circumstances. Interpretation of "exceptional circumstances" shall be the responsibility of the college authorities.

PROCUREMENT AND ASSIGNMENT SERVICE FOR PHYSICIANS, DENTISTS AND VETERINARIANS

INTERN-RESIDENT PROGRAM FOR HOSPITALS

Considerable confusion seems to have arisen regarding the number of internships and residencies which may be maintained by hospitals under the new intern-resident program which has been made possible by the deferment of certain numbers of interns and residents holding reserve commissions in the Army and Navy.

To meet the minimum needs of hospitals nationally, twice as many residents as will be deferred by the Army and Navy will be required. The remaining half (those not deferred by the Army and Navy) must be made up of physically disqualified men and women in order to give the hospitals minimum adequate house staff coverage.

This program definitely does not state that a hospital may only, or will necessarily, retain one third of its interns to serve as junior residents, nor does it mean that a hospital may only, or will necessarily, retain one half of its junior residents as senior residents. These fractions were published to show the overall proportion of commissioned officers now under the jurisdiction of the Army and Navy who would be deferred by the military services to serve as one source of personnel for civilian hospital appointments.

The program does state that, generally speaking, hospitals will be able to retain about two thirds of their 1940 house staffs, provided there has been no pronounced decrease or increase in patient load since that time. This two thirds will comprise those ineligible for military service as well as those deferred by the Army and Navy.

The first fraction represents the proportion of deferments by the armed forces of commissioned officers (9-9-9). The second figure concerns the allocation—the combined deferred officers and those physically disqualified—to the hospitals (approximately 66⅔ per cent of the 1940 staff). Each hospital should procure as many physically disqualified men as possible, and only the remainder unable to be procured from this source can be obtained from those deferred by the Army and Navy.

The hospital questionnaires, which the Procurement and Assignment Service urgently requests hospitals to return, will give the needed information to determine a general basis for estimating the number of interns and residents which each hospital should have on the basis of the 1940-1942 house staff. There will probably be some necessary changes in individual hospitals which have peculiar or particular problems, but the formula will apply to all general hospitals.

MISCELLANEOUS

NATIONWIDE CAMPAIGN FOR QUININE

In a nationwide campaign which began seven months ago for the conservation of quinine for the armed forces, more than eleven million 5 grain doses of quinine have been collected and are now en route to army and navy fighting fronts. The campaign was supported by thousands of retail pharmacists, wholesale druggists and hospitals and exceeded its goal by nearly 50 per cent. More than sixteen thousand packages have been received at the National Quinine Pool, American Pharmaceutical Association, Constitution Avenue and Twenty-Second Street N.W., Washington, D. C. The quinine arrived in the form of powder, plain and sugar coated tablets, crystals and liquid and was of both foreign and domestic manufacture. The medical departments of the Army and Navy have assigned pharmacists to assort and classify the contributions, which will be accepted until October 15.

NEW FEE SCHEDULE FOR THE EMERGENCY MATERNITY AND INFANT CARE PROGRAM

Under a new fee schedule effective August 18, medical care was authorized for 974 wives and children of enlisted men of West Virginia for the first fifteen weeks' operation of the plan proposed by the state health department for the emergency Maternity and Infant Care Program. This plan was approved by the Children's Bureau of the Labor Department in Washington. As of August 19, a total of 361 West Virginia doctors had qualified for participation in this program, which is under the direct supervision of Dr. Lenore Patrick, director of the Division of Maternal and Child Hygiene. Fifty-five approved hospitals were taking part.

SCHOOLS DETERMINE POLICY IN REGARD TO MARRIAGE OF MEMBERS OF THE U. S. CADET NURSE CORPS

According to the Division of Nurse Education of the U. S. Public Health Service, in many schools marriage does not prevent the admission and retention of students. In some schools maternity leave is granted; in a few schools married applicants are not admitted and married students are not retained. The fact that a school is receiving federal funds under the Bolton act does not alter a school's policy in regard to marriage. An applicant, before enrolling in any school of nursing as a U. S. cadet nurse, should understand the school's policy on marriage. If a school admits and retains married students, the "health permitting" clause in the application signed by the cadet nurse allows the school to provide maternity leave. This clause applies in the same fashion to the graduate nurse who has pledged herself to render essential nursing service throughout the war. Students who are enrolled in schools in which marriage of students is prohibited, if they wish to marry before completion of the program, might consider the possibility of transfer to another school, although the preferable course to follow would be that of waiting to marry until after graduation.

PUBLIC HEALTH UNDER HITLER

The Greek government has decided to supply all consumptives insured at social insurances with better food consisting of meat, eggs, sugar and butter, *Donauzeitung*, Belgrade, July 16, reports. Previously this allowance was granted in grave cases only. In Athens consumptives are estimated to number 20,000.

According to DNB of July 24 a commission sent by the Spanish minister of labor to study the German health insurance system is at present staying in Berlin. The members of the commission have the task of acquainting themselves with the statutory regulations and the organization of German health insurance. The Spanish government intends to introduce a health insurance system in Spain. The Spanish visitors will have the opportunity to study all institutions concerned in the great German reich and in the protectorate and to acquaint themselves with the working of the German health insurance system. The reich minister of labor, Franz Seldte, received the members of the commission. In his address he spoke of his pleasure at Spain's intentions to organize a health service for the Spanish workers. The reich ministry of labor would gladly cooperate to help Spain to realize these aims.

12-Uhr Blatt of July 10 prints a description of the largest underground hospital in Berlin. Operations are carried out in this hospital every night in order to be prepared in case of an emergency. Expectant mothers are accommodated here every night and many babies have already been born in this hospital.

Rumania *Curentul* of July 22 states that medical students must do one month's military service plus one month's medical practice during the summer vacation.

ORGANIZATION SECTION

MEDICAL LEGISLATION

MEDICAL BILLS IN CONGRESS

Change in Status.—H. J. Res. 159 has passed the House and has been favorably reported without amendment by the Senate Committee on Appropriations, making available an additional sum of $18,620,000 to provide obstetric and pediatric care to the wives and infants of enlisted men of the fourth, fifth, sixth and seventh grades in the armed forces of the United States. An effort was made on the floor of the House to amend the joint resolution so that the federal money could be made available in the form of allotments to the wives of servicemen, but the amendment was defeated by a vote of 115 to 8.

Bills Introduced.—The President has submitted to Congress a supplemental estimate of appropriation for the Veterans' Administration, for the fiscal year 1944, in the amount of $10,356,000, to provide 3,950 additional beds for neuropsychiatric patients at thirteen existing facilities of the Veterans' Administration (H. Doc. 280). H. R. 3204, introduced by Representative Lynch, New York, undertakes to provide a system of old age and survivors' insurance for employees of certain organizations not at present within the coverage of the Social Security Act, such as religious, charitable, educational and scientific organizations. H. R. 3293, introduced by Representative Peterson, Florida, provides that, nothwithstanding any provision of law or veterans' regulation, the pension, compensation or retirement pay of a veteran of the war with Spain, including the Philippine Insurrection and the Boxer Rebellion, shall not be reduced while such veteran is being furnished hospital treatment or institutional or domiciliary care by the United States or any political subdivision. H. R. 3294, introduced by Representative Talbot, Connecticut, provides that any blind person who is traveling on a train being operated by any common carrier by railroad subject to the Interstate Commerce Act may keep his seeing eye dog with him in any coach or Pullman car of such train.

DISTRICT OF COLUMBIA

Change in Status.—S. Res. 178 has been agreed to, authorizing the Senate Committee on the District of Columbia to investigate conditions at Gallinger Municipal Hospital, with particular reference to sanitation, food, diet and the treatment and care of tuberculous patients. The committee will be authorized to call on the United States Public Health Service for such professional, technical or other assistance as it may deem necessary for the purposes of the investigation.

Bills Introduced.—S. 1340, introduced by Senator McCarran, Nevada, proposes to establish a sanitary code governing the operation of restaurants in the District of Columbia. Among other things the bill provides that, when suspicion arises as to the possibility of transmission of infection from any restaurant employee, the health officer will be authorized to require (1) the immediate exclusion of the employee from all restaurants and (2) the immediate closing of the restaurant concerned until no further danger of disease outbreak exists. H. R. 3314, introduced by Representative Randolph, West Virginia, provides for the disposition of funds collected by District of Columbia examining, licensing and other boards and commissions, including the Commission on Licensure to Practice the Healing Art.

MEDICAL ECONOMIC ABSTRACTS

OHIO RURAL MEDICAL SERVICE PLAN

Several governmental and private organizations asked the Ohio State Medical Society to join in setting up a prepayment medical service plan for farmers in Logan County. The council of the Ohio State Medical Society asked the Public Relations Committee to investigate the situation. The chairman of that committee submitted the following recommendation, which was adopted by the council: [1]

"That the council authorize the use of an amount, not to exceed $15,000, from the reserve fund of the association for the organization and establishment of a medical service plan in Logan County under the terms of the Ohio Enabling Act, provided the establishment of a plan in that county has the approval and active support of the Logan County Medical Society; that $10,000 of this amount would be advanced for the purpose of meeting the financial provisions of the Enabling Act and that the balance would be used under the direction of the Committee on Public Relations and Economics for preliminary organizational work and activities."

In submitting the foregoing recommendation, Dr. Hein pointed out that the question will be discussed by the Logan County Medical Society as soon as that society is informed as to what assistance, financial and otherwise, the Ohio State Medical Association will contribute.

1. Proceedings of the Council, Ohio State M. J. **39**: 756 (Aug.) 1943.

WOMAN'S AUXILIARY

Louisiana

The annual meeting of the Woman's Auxiliary to the Louisiana State Medical Society was held in Baton Rouge recently with the president, Mrs. Clarence B. Erickson, presiding. Mrs. Richard H. Clark, president of the Southern Medical Association auxiliary, and Mrs. Sam Houston, wife of the governor of Louisiana, were guests of honor. Mrs. Houston extended an invitation to all those present to attend a reception at the executive mansion that evening.

Dr. Emmet Irwin, president of the Louisiana State Medical Society, visited the auxiliary meeting and outlined plans for the coming year. Mrs. George Taquino is the incoming president and Mrs. Rhodes Spedale is the president-elect.

Colorado

The board of the Woman's Auxiliary to the Denver County Medical Society has asked each member to contribute $2.38 in excess of dues to the student loan and emergency funds this year. The fund will be used to assist medical students who are unable to pass the Army or Navy physical requirements and who are on their own resources to complete a medical education. The emergency fund is to be available for use in aiding the families of young doctors in service.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

CALIFORNIA

Gift for Library.—Dr. Theodore S. Kimball, pathologist of the 47th General Hospital group, Modesto, recently presented the White Memorial Medical Library of the College of Medical Evangelists, Los Angeles, with $500 to buy books for the hematology section of the library. Dr. Kimball was associate professor of pathology at the College of Medical Evangelists.

Universities and the Medical Profession.—The San Francisco County Medical Society devoted its September 14 meeting to a discussion of "The Universities and the Medical Profession." The speakers were Drs. Loren R. Chandler, dean, Stanford University School of Medicine, on "The Place of the Practicing Physician in Medical Schools"; Francis Scott Smyth, dean, University of California Medical School, "Some Features of Medical Education Under the Present Circumstances," and Donald B. Tresidder, president, Stanford University, "Some Major Problems of Education Confronting a Private University Now and In the Postwar Period."

Public Health Officials and Industrialists Cooperate.—A committee called the Industrial Division of the City of Los Angeles and County Defense Council has been formed to bring about a closer understanding by public health officials in the area and the industrialists. The tentative program of the committee aims (1) to establish and maintain an advisory council of public health officers and representatives of the private medical profession; (2) to provide a common point of initial contact for industrial management on all problems of industrial health; (3) to effect practical procedures for prompt reference of these problems to the proper medical authorities, and (4) to undertake an educational campaign, using the press, radio and direct mail to convince industrial management and employees (*a*) of the importance of preventing interference with the war production program by preventable employee illnesses, (*b*) of the possibility of serious epidemics under present and anticipated conditions of housing and inadequate nourishment and resulting from the migration of workers from other sections of the country where health supervision has not been provided, (*c*) of the necessity for preemployment medical examination not as a basis of applicant exclusion but, first, to aid persons with communicable diseases to contact corrective medical procedures and, second, to assure the placement of new employees in occupations suitable to their health status, and (*d*) of the advisability of providing continuing medical inspections to discount the possibility of the spreading of diseases into industry from outside sources.

DISTRICT OF COLUMBIA

Personal.—Mr. Edward K. Funkhouser has been appointed executive secretary of the District Tuberculosis Association. According to *Medical Annals,* Mr. Funkhouser has served for the past eighteen years as executive secretary of the Passaic County, N. J., Tuberculosis and Health Association.—Dr. Charles C. Chapple has been appointed chief medical gas officer in the Office of Civilian Defense, and Abraham N. Franzblau, P. A. Surgeon, U. S. Public Health Service, has been relieved as acting medical gas officer to be assigned as assistant to the chief medical officer.

New Blood Donor Center.—The dedication of the new District Red Cross blood donor center at the Acacia Building, Washington, took place on July 31. The center is operated under the direction of the District Red Cross and is staffed by Army and Navy medical officers and Red Cross personnel, both paid and volunteer. Lieut. Eugene W. Higgins (MC), U. S. Naval Reserve, is physician in charge. The invocation was delivered by Capt. Robert D. Workman, chief of the navy chaplains, and the speakers included Major Gen. Norman T. Kirk, surgeon general of the U. S. Army, Rear Admiral Harold W. Smith (MC), U. S. Navy, and Fred M. Vinson, director of economic stabilization, who read an address by James F. Byrnes, director of war mobilization. The center is housed in the building of the Acacia Mutual Life Insurance Company, which presented space for the center to the Red Cross.

FLORIDA

Time Limit Set to Register Medical Licenses.—Licenses to practice medicine in Florida must henceforth be registered within sixty days of the date shown on the license, in accordance with an amendment to the Florida statutes which became effective June 11. The original law required that every license to practice medicine be registered in the office of the clerk of the circuit court of the county in which the licensee resides or in which his practice is intended to be carried on, but no time limit was specified. Licenses have been recorded as late as twenty years after the date of issuance. All unregistered licenses which were in effect on June 11 of this year, when the new law became effective, must be recorded within six months of that date. It is expected that the new law will help prevent the recording of fraudulent licenses.

ILLINOIS

Occupational Therapy.—A new curriculum on occupational therapy has been set up by the University of Illinois. Students will spend their first five semesters of study on the Urbana-Champaign campus and four semesters in the college of medicine, Chicago.

Botulism Antitoxin Now Available.—The state department of public health is now making available to Illinois physicians, without charge, botulism antitoxin, combined types A and B, for emergency use in the care of persons who have eaten food that is so poisoned. The antitoxin may be obtained from the department's offices at Springfield and from the department's laboratories at Carbondale, Champaign and Chicago.

Dr. Fitzgerald Named Supervising Ophthalmologist for Public Aid Commission.—Dr. James Robert Fitzgerald, clinical associate in ophthalmology, Loyola University School of Medicine, Chicago, has been appointed supervising ophthalmologist of the Illinois Public Aid Commission. In this capacity he will review the reports made of examining ophthalmologists on applicants for aid under the blind assistance program and will determine the eligibility of these applicants on the basis of loss of sight. He will also provide the commission's staff with technical advice on general policy and on individual problems in the administration of the program. Initial grants under the program, which is being financed jointly by the state and federal governments, were to be started on October 1. Under the program, aid will be furnished on the basis of need to blind residents of Illinois who are 18 years of age and over. Where possible, treatment will be given to restore the sight of recipients of this aid. Special efforts will be made to assist recipients to become self supporting.

Chicago

Dr. William Hibbs Made Medical Director at Presbyterian.—Dr. William G. Hibbs, associate clinical (Rush) professor of medicine, University of Illinois College of Medicine, has been appointed medical director of Presbyterian Hospital. He began his work on August 1. Dr. Hibbs graduated at Rush Medical College in 1920 and served his internship at Presbyterian, where he has been a member of the regular staff since 1925. He represents the American Medical Association on the joint committee on hospital library service.

Nutrition in Wartime.—The Institute of Medicine of Chicago will conduct a postgraduate assembly on "Nutrition in Wartime," November 17-18. The program will be devoted to phases of nutrition that are of particular interest to practicing physicians, dentists, nutritionists and dietitians. Among the speakers will be:

Frank L. Gunderson, Ph.D., Washington, D. C., The Impact of the War on the Diet of the City and Rural Dweller.
Dr. Leonard G. Rowntree, Washington, D. C., The State of Nutrition in Urban and Rural Populations as Reflected by Selective Service Rejections.
Dr. John B. Youmans, Nashville, Tenn., Early Clinical Recognition of Nutritional Deficiencies.
Dr. Paul R. Cannon, Chicago, Some Pathologic Aspects of Undernutrition.
William A. Perlzweig, Ph.D., Durham, N. C., Laboratory Aids in the Evaluation of Nutritional Deficiencies.
Lydia J. Roberts, Ph.D., Chicago, Present Day Concepts of Nutritional Requirements.
William C. Rose, Ph.D., Urbana, Ill., The Role of Protein in the Diet.
Dr. George H. Whipple, Rochester, N. Y., Food Proteins, Blood Proteins and Disease Therapy.
Dr. Samuel Soskin, Chicago, The Role of Carbohydrate in the Diet.
Dr. Anton J. Carlson, Chicago, Some Obstacles in the Path Toward an Optimum Diet.
Dr. Julian D. Boyd, Iowa City, Teeth as An Index of Nutrition, Icie Macy Hoobler, Ph.D., Detroit, Nutritional Requirements in Normal Pregnancy and Lactation.
Dr. Edward H. Rynearson, Rochester, Minn., Overweight and Underweight.
Dr. Henry T. Ricketts, Chicago, The Use of Carbohydrate in the Treatment of Disease.
Dr. Morris Fishbein, Editor of THE JOURNAL, Uses and Abuses of Vitamins.

There will be six panel discussions on therapeutic diets and rationing, current practices in infant feeding, parenteral nutrition: methods and indications, the proper place of accessory vitamins in the diet, can dental caries in the young and in pregnant women be controlled by diet? and controversial aspects of diet in diabetes. Another feature will be a "Nutrition Information Please" with Dr. Fishbein acting as moderator and Drs. Gunderson, Perlzweig, Rose, Rowntree, Whipple and Youmans comprising the board of experts.

INDIANA

Dr. Lawson Observes Ninety-Fourth Birthday. — Dr. Wilson T. Lawson, Danville, said to be the oldest practicing physician in Indiana and the oldest living graduate of Wabash College, Crawfordsville, observed his ninety-fourth birthday on September 3. Dr. Lawson is health officer of Hendricks County and still takes care of his own office work, making some calls, newspapers report.

Personal.—Frank G. Laird, who has been acting as president of the Indianapolis Board of Health since the retirement of Dr. Maurice J. Barry, was elected president of the board at the annual business meeting on July 16. Dr. Leonard A. Ensminger was elected vice president and Dr. Herman G. Morgan was elected secretary and city health officer for the thirty-second year.——Dr. Charles C. Crampton, Delphi, on June 22 observed his completion of fifty years in the practice of medicine. His associates in the Arnett-Crockett Clinic in Lafayette presented him with a diamond pin denoting that he had served as commander of the American Legion. He has been a past president of both the Monon and Wabash railroaders associations, of the county medical society and of the eleventh councilor district of the state medical society.——Dr. Stanley A. Dowiat, Cicero, Ill., has been appointed superintendent of the Smith-Esteb Memorial Hospital, Richmond, to succeed Dr. Henry Vernon Madsen, resigned.——Philip S. Winnek, formerly of Stamford, Conn., has become director of research of Pitman-Moore Company, Indianapolis, pharmaceutic and biologic manufacturers.

MASSACHUSETTS

Dr. Harry Solomon Named Professor of Psychiatry at Harvard.—Dr. Harry C. Solomon, clinical professor of psychiatry, has been appointed professor of psychiatry at Harvard Medical School and medical director of the Boston Psychopathic Hospital, succeeding the late Dr. C. Macfie Campbell. Dr. Solomon graduated at Harvard in 1914 and has been on the faculty there since 1915.

Grant for Work in Immunochemistry.—The Rockefeller Foundation has awarded a grant to William C. Boyd, Ph.D., associate professor in biochemistry, Boston University School of Medicine, to enable him to continue his research work in immunochemistry for a two year period. A former grant received from the Guggenheim Foundation enabled Dr. Boyd to do original research in Egypt. He graduated at Harvard University, Boston, in 1925. He has been a teaching fellow in the Boston University School of Medicine since 1926 and received his Ph.D. there in 1930.

MICHIGAN

Personal.—Dr. Edward L. Collins, Grand Rapids, has been appointed superintendent for the Michigan Institute for the Blind at Saginaw. Dr. Collins has been blind since a child. ——Dr. Albert A. Hughes, Detroit, has been elected Most Worshipful Grand Master of Michigan Masonry.——Dr. David H. Burley recently completed fifty years of practice in Almont; he is also a registered pharmacist. —— Dr. Wesley H. Mast, Petoskey, has been appointed a member of the state advisory council of health for a six year term ending June 30, 1949.—— Dr. Leslie E. Coffin, Painesdale, was installed as president of the Upper Peninsula Medical Society at its recent meeting in Iron Mountain and Dr. Nathan J. Frenn, Bark River, was chosen president-elect. Dr. Robert J. McClure, Calumet, secretary of the Houghton-Baraga-Keweenaw County Medical Society, will be the secretary of the Upper Peninsula Medical Society during the ensuing year.

Committees on Workers' Health.—The Michigan State Medical Society and the United Auto Workers have agreed to set up committees to confer on medical and health problems of Michigan's industrial workers, newspapers report. Members of the committee appointed by the state medical society include Drs. Robert L. Novy, Detroit, chairman; Gustave L. McClellan, Detroit; Patrick L. Ledwidge, Detroit; Earl F. Carr, Lansing; Samuel W. Donaldson, Ann Arbor, and Otto K. Engelke, Ann Arbor. The formation of the United Auto Workers C. I. O. committee had not been completed at the time of this report, but tentative plans indicated that George F. Addes, secretary-treasurer of the U. A. W.-C. I. O., will be ex officio chairman. The arrangement was worked out after an appeal had been submitted to the medical society by the union for a list of medical and surgical specialists who would accept patients referred by the union's own medical department.

MISSOURI

Personal.—Robert Bruce Moffett, Ph.D., since 1941 postdoctorate research associate at Northwestern University, has been appointed senior research chemist in the laboratories of George A. Breon & Company, Kansas City.——Dr. Richard E. Banner, Kansas City, has been named head of the health unit in Johnson County with headquarters at Warrensburg.

Grant to Finance Research in Caudal Anesthesia.—The U. S. Public Health Service has made a grant to Washington University School of Medicine, St. Louis, to help finance a cooperative study of the gross anatomy of the spinal dura mater and the conformation of the posterior surface of the sacrum. The project is under the supervision of Mildred Trotter, Ph.D., and Dr. Virginia S. Lanier of the department of anatomy and Dr. Howard E. McKnight of the department of obstetrics and gynecology. It is anticipated that the results will be a contribution to the procedure of the administration of continuous caudal anesthesia in childbirth.

NEW JERSEY

State Department Creates Tuberculosis Division.—The New Jersey State Department of Health has organized a division of tuberculosis to combat a sharp increase in the disease in the industrial areas. According to the Bulletin of the National Tuberculosis Association, 507 cases of tuberculosis have been found in 42,000 chest x-ray films taken in nine industrial areas of the state.

Industrial Physicians Wanted. — The Department of Health of the State of New Jersey, Trenton, whose industrial health activities have expanded rapidly during the present war, has announced its need for two full time industrial hygiene physicians for its industrial hygiene service. The principal duties of the selected physicians will be consultations in regard to the control of occupational diseases, industrial toxicologic problems, evaluation of adequacy of plant medical services, promotion of measures which will reduce absenteeism from nonoccupational causes, and conduct of industrial health education activities.

NEW YORK

Fifty Years of Practice.—The *News Letter* of the Suffolk County Medical Society for September was dedicated to members who had completed a half century in the practice of medicine and who participated in a celebration in July. The members who were honored include Drs. William Newton Barnhardt, Toronto, Ont.; George Herbert Carter, Huntington; William Elliott Foster, Babylon; Frank Diah Peterson, Cutchogue, and Frank Overton, Patchogue.

Personal.—Dr. Theodore G. Klumpp, president of the Winthrop Chemical Company, has been elected a member of the Academia de Ciencias Medicas, Fisicas y Naturales de la Habana, Cuba. Presentation of the academy's medal will take place at a future date in Havana, where Dr. Klumpp will go to deliver a scientific paper.——Dr. Thomas M. Holmes, Delmar, has been appointed a member of the medical board of the State Employees Retirement System, succeeding Dr. Clarence E. Mullens, Albany.

Dr. Burton Simpson Retires from State Institute.—Dr. Burton T. Simpson, director of the State Institute for the Study of Malignant Diseases, Buffalo, retired on August 1 after having reached the compulsory retirement age. He had been in the service of the state since 1910, first as resident pathologist of the institute and since 1924 as its director. In 1931 he was appointed director of the newly created division of cancer control, combining the duties of that position with those of the administration of the institute. He continued until 1939, when the division was reorganized and its headquarters transferred to Albany, primarily to amplify the resources available to practicing physicians throughout the state for the diagnosis and care of cancer. Since then Dr. Simpson has devoted full time to administering the institute. He was president of the American Society for the Control of Cancer in 1935.

PENNSYLVANIA

University Bulletin Honors Oldest Graduate.—The *Pennsylvania Gazette*, official journal of the University of Pennsylvania, Philadelphia, paid special tribute in its September issue to Dr. John A. Fell, Doylestown, who is 93 years of age and the oldest living graduate of the university's medical school. Dr. Fell graduated at the medical school in 1874. He is also the oldest living graduate of Lafayette College, which he attended two years before entering Pennsylvania. After graduating from the Doylestown English and Classical Seminary Dr. Fell taught school for two years and was principal of the Hughesian Free School, Buckingham. He not only has served his community for many years as a practicing physician but also has been a member of the Doylestown School Board, the Doylestown Board of Health and at one time served as assistant surgeon of the Sixth Regiment of the Pennsylvania National Guard. In 1933 the state medical society paid tribute to him in recognition of his "fifty-nine years of medical service faithfully performed to his community in the traditional ideals of the medical profession."

Pittsburgh

Colonel Dabney Named Assistant Dean.—Col. Albert S. Dabney, M. C., U. S. Army, assistant commandant of the Medical Field Service School at Carlisle Barracks, Pennsylvania, has been appointed assistant dean at the University of Pittsburgh School of Medicine, effective October 1. Colonel Dabney was relieved from his duties at Carlisle Barracks on August 31 in order to take advantage of accrued leave before being placed on the compulsory retirement list, November 30, at the age of 64. Col. Guy B. Denit, M. C., U. S. Army, who recently returned from a six months tour of duty as chief surgeon of a base section in the African theater of operation, will temporarily replace Colonel Dabney as assistant commandant at the field service school. A ceremonial retreat parade was held on August 31 in honor of Colonel Dabney, and Brig. Gen. Addison D. Davis, commanding general of Carlisle Barracks, commended Colonel Dabney for his loyal and efficient services. A veteran of two world wars and a medical officer for twenty-seven years, Colonel Dabney had been at Carlisle Barracks since June 27, 1939, first as director of the medical department equipment laboratory and on Jan. 10, 1942 as assistant commandant. Previous to his service at Carlisle Barracks he had been executive officer in the Surgeon General's Office at Washington, D. C.

SOUTH CAROLINA

Personal.—Dr. Luther A. Riser, Sedgefield, N. C., has been named director of the bureau of vital statistics of the state board of health to succeed Dr. Martin B. Woodward, Aiken, who resigned to accept a similar position in West Virginia.——A bronze bust of Dr. Frank H. McLeod, founder of the McLeod Infirmary at Florence, was recently presented to the infirmary to mark his many years' service to the community. Although not in practice, Dr. McLeod still serves as medical superintendent of the infirmary.

Refresher Course.—The Alumni Association refresher course of the Medical College of the State of South Carolina, Charleston, inaugurated last year, will be held November 3-4 at the Baruch Memorial Auditorium, Charleston. Speakers will be:

Dr. Harrison F. Flippin, Philadelphia, The Uses and Abuses of the Sulfonamides.
Dr. Charles C. Wolferth, Philadelphia, Differential Diagnosis of the Anginal Syndrome.
Dr. Leroy U. Gardner, Saranac Lake, N. Y., The Essentials of Pneumoconiosis.
Dr. Alfred Blalock, Baltimore, Traumatic Shock.
Dr. Virgil P. W. Sydenstricker, Augusta, Ga., Deficiency Diseases.
Dr. George W. Thorn, Boston, Physiologic Considerations in the Treatment of Nephritis.
Dr. J. T. King, Washington, D. C., Calcific Aortic Stenosis.
Dr. Roy R. Kracke, Emory University, Ga., Diagnosis and Treatment of the Hemorrhagic Diseases.

There will be round table discussions on "The Sulfonamides," "Treatment of Heart Disease," "Pulmonary Diseases" and one on "Thyroid Disturbances." Surgical round table discussions will be held, as will pathologic conferences. At the founder's day banquet, Thursday evening, Dr. Henry E. Meleney, New York, will discuss "Tropical Medicine, Present and Future."

Investigation of Medical Education and Medical Service Launched.—The investigation of medical education and medical service in South Carolina started on August 25 in the senate chamber when a specially selected joint committee met to begin the taking of testimony. The committee is composed of Senators James E. Leppard, Chesterfield, chairman, O. T. Wallace, Charleston, and C. S. McCall, Marlboro; Representatives J. Claude Fort, Cherokee, and James B. Morrison, Georgetown; and from the medical association Dr. Walter R. Mead, Florence, and Dr. William R. Wallace, Chester. Morning and afternoon sessions were held. It is expected that another meeting will be held in Charleston and probably a third in Columbia, after which a report will be made to the general assembly in January. The committee, under a resolution creating it, is to ascertain the cause of "present acute shortage of medical doctors and medical services in this state" and recommend "such measures as shall be necessary to procure and maintain an adequate supply and proper distribution of physicians and surgeons" and also to determine whether the state medical college in Charleston "should be enlarged so as to provide a sufficient supply of medical doctors to serve the needs of the state" and also whether a medical college should be established at the University of South Carolina. The committee is also to determine "whether it is necessary or desirable that the state should subsidize the cost" of educating medical students and whether it is necessary "for the state to provide in whole or in part public medical services." Among those appearing before the committee at this first meeting were Dr. Robert Wilson, dean of the medical college of the state, Dr. Kenneth M. Lynch, chairman of the state board of health and Dr. Carl B. Epps of Sumter (THE JOURNAL, July 10, p. 757).

TENNESSEE

New Health Set Up in Nashville.—Dr. Thomas V. Woodring, assistant health officer of Nashville for more than fifteen years, has been appointed director of health of Nashville, a position recently created under a revision of the charter for the city. Dr. John Overton will continue as city health officer. The creation of the position of director of health was a recommendation of the public administration service to obtain a better and more efficient government.

Personal.—Mrs. Dorothy Davis Bryan, Nashville, has been appointed to succeed the late Dr. Hale E. Cullom as director of sight conservation and prevention of blindness for the state of Tennessee.——New appointments to the Public Health Council include those of Dr. Walker L. Rucks, Memphis, and Dr. Thomas R. Ray, Shelbyville. Dr. Rucks succeeds Dr. Webster B. Key, who is now a lieutenant commander in the U. S. Naval Reserve.——Dr. David Galloway, Memphis, has been appointed superintendent of the Western State Hospital.

WISCONSIN

Physician Named to New Veteran Recognition Board.—Dr. Charles A. Dawson, River Falls, has been appointed by Acting Governor Goodland as a member of the newly created Veteran Recognition Board. The state medical journal reports that the board will have charge of handling the $6,300,000 earmarked by the legislature for the educational, medical and economic rehabilitation of World War II veterans of Wisconsin and their families, as well as any other state or federal funds set aside for such rehabilitation. Members of the board will receive no salary for their services but will be paid their expenses. A director and staff will be created to administer their funds, the staff to be under civil service.

The Dr. William Beaumont Foundation.—At the first meeting of the Dr. William Beaumont Memorial Foundation in Prairie du Chien, September 18, Dr. William D. Stovall, Madison, director of the state laboratory of hygiene, was elected chairman of the board of directors and M. J. Dyrud, Prairie du Chien, was chosen president. The foundation was incorporated in May and its purpose is to "perpetuate the name and memory of Dr. Beaumont and his memorable experiments in the physiology of digestion, and to recognize noteworthy contributions made by other physicians and surgeons of the United States." Organization of the foundation was planned and carried through by the Crawford County Medical Society and the local Kiwanis club. Other officers include Dr. Olaf E. Satter, vice president, Dr. Thomas F. Farrell, treasurer, and J. Alvin Dru'yor, secretary, all of Prairie du Chien. Other members of the board of directors are Mayor F. W. Clanton, F. A. Otto and Paul H. Schmidt, all of Prairie du Chien. Walter J. Meek, Ph.D., acting dean of the University of Wisconsin Medical School, Madison, was appointed chairman of the advisory board by the directors at their meeting after the membership meeting. Other appointments made by the board of directors were Cal Peters, curator; Dr. Peter L. Scanlan, Dr. Henry H. Kleinpell, Dr. John J. Kane, Dr. Charles A. Armstrong and Dr. Emil H. Lechtenberg, medical advisers to the curator, and Mr. Dyrud, general manager. The first meeting of the new foundation was held in the hospital section of the second Fort Crawford, built in 1829, in which Dr. Beaumont served as post surgeon under Col. Zachary Taylor, then commandant at the fort. This building, which is now owned by

the city of Prairie du Chien and leased by the D. A. R., is being considered as the home of the foundation. Tentative plans call for the restoration of the building to its original state as it was when Dr. Beaumont was in charge. Dr. Beaumont performed fifty-six of his noted experiments on Alexis St. Martin in the hospital section of Fort Crawford between 1826 and 1832. A number of important books and papers of Dr. Beaumont's are available in Prairie du Chien and will be turned over to the foundation when it has a suitable home.

GENERAL

Better Parenthood Week. — The sixth annual Better Parenthood Week will be observed nationally, October 25-31. Parent-teacher, child care, welfare and various civic organizations and study groups will cooperate through programs dealing with parent and child care problems, especially those which confront the nation during wartime.

International Medical Assembly. — The twenty-eighth annual International Medical Assembly of the Inter-State Postgraduate Medical Association of North America will be held at the Palmer House, Chicago, October 26-29, under the presidency of Dr. Frank H. Lahey, Boston. Among the speakers will be:

Dr. Edmund B. Spaeth, Philadelphia, Removal of Metallic Foreign Bodies from the Eyeball and from the Orbit.
Dr. James L. Poppen, Boston, The Management of Ruptured Intervertebral Disks.
Dr. George B. Eusterman, Rochester, Minn., The Treatment of Gastric and Duodenal Ulcer.
Dr. Fraser B. Gurd, Montreal, Canada, Treatment of Burns.
William H. Headlee, Ph.D., Indianapolis, Precautions Against the Introduction of Tropical Diseases into the United States.
Dr. Major G. Seelig, St. Louis, The Talcum Problem in Surgery and Its Solution.

At the assembly dinner Dr. Lahey will discuss "Some of the Problems of the War" and Brig. Gen. Fred W. Rankin, M. R. C., "Current Considerations of Postgraduate Medical Education."

Dearholt Medal Awarded.—Will Ross, president of Will Ross, Inc., Milwaukee, was presented on September 8 with the Dearholt Medal awarded annually by the Mississippi Valley Conference on Tuberculosis. The medal is awarded for outstanding work and service in combating tuberculosis. Mr. Ross was a patient in a sanatorium founded by the late Dr. Hoyt E. Dearholt, for whom the medal is named, and in 1911 published a book titled "My Personal Experience with Tuberculosis." New officers of the Mississippi Valley Conference include Mrs. Blanche H. de Koning, executive secretary of the Grand Rapids Anti-Tuberculosis Society, Grand Rapids, Mich., president; Dr. Robert H. Hayes, Chicago, a member of the board of directors of the Tuberculosis Institute of Chicago and Cook County, vice president, and A. W. Jones, executive director of the St. Louis Tuberculosis and Health Society, St. Louis, secretary-treasurer. Officers of the Mississippi Valley Trudeau Society, which met jointly with the conference, are Dr. Loren L. Collins, Ottawa, Ill., president-elect; Dr. Henry S. K. Willis, Northville, Mich., president; Dr. Oscar Lotz, Milwaukee, vice president, and John H. Scavlem, Cincinnati, secretary-treasurer.

American Public Health Association. — The seventy-second annual business meeting of the American Public Health Association and its wartime public health conference will be held at the Hotel Pennsylvania, New York, October 11-14. An extensive program has been prepared covering public health and including general sessions and section meetings. A special session will be held Tuesday afternoon on "New Ventures Toward Health Security," at which the speakers will include Nathan Sinai, D.P.H., Ann Arbor; Dr. John J. Heagerty, Ottawa, Ont., and Homer Folks, LL.D., New York. "Latin America Looks Toward the Future" will be discussed by a speaker to be announced later. A second special session will be held Wednesday on "Public Health Implications of Tropical and Imported Diseases" at which the speakers will be Dr. Henry E. Meleney, New York; Dr. Wilbur A. Sawyer, New York; Surg. Gen. Thomas Parran of the U. S. Public Health Service, and one other to be announced later. On Wednesday afternoon a special session will be devoted to "Current Health Department Problems in War," the panel leader to be Dr. Huntington Williams, Baltimore. Thursday a special session will be devoted to "The Evolving Pattern of Tomorrow's Health," the speakers to be Dr. Joseph W. Mountin, Washington, D. C.; Dr. William P. Shepard, San Francisco; C.-E. A. Winslow, Dr.P.H., New Haven, Conn.; Henry F. Vaughan, Dr.P.H., Ann Arbor, and Dr. Felix Hurtado. Other features at the meeting will include symposiums on cancer, on the impact of the war on sanitary engineering, the recent developments in sanitary engineering, postwar opportunities and responsibilities of the sanitary engineer and on gonorrhea. Other speakers will include:

Selman A. Waksman, Ph.D., New Brunswick, N. J., Antibiotic Substances, Production by Micro-Organisms, Nature and Mode of Action.
Colonel Edgar Erskine Hume, M. C., U. S. Army, The Problem of Rickettsial Diseases Among the Armed Forces.
Dr. Felix J. Underwood, Jackson, Miss., Planning Today for Public Health Administration Tomorrow.
Dr. Carl A. Wilzbach, Cincinnati, Results of Medical and Dental Examinations of 2,500 Senior High School Students.
George R. Cowgill, Ph.D., New Haven, Conn., Nutrition—A Factor Important for Industrial Hygiene.
Dr. Frank G. Boudreau, New York, Food and Nutrition Policy Here and Abroad.

Other groups meeting at this time will include the American School Health Association, the American Social Hygiene Association and on Monday an inter-American conference on health education.

Academy of Ophthalmology and Otolaryngology.—The annual session of the American Academy of Ophthalmology and Otolaryngology will be held at the Palmer House, Chicago, October 10-13, under the presidency of Dr. James A. Babbitt, Philadelphia. Among the speakers will be:

Dr. Harry S. Gradle, Chicago, A Program of Ophthalmic Service for Small Plants.
Dr. Alson E. Braley, New York, Epidemic Keratoconjunctivitis: Results of Therapy.
Dr. Walter B. Lancaster, Boston, The Present Status of Eye Exercises for Improving Visual Functions.
Dr. William F. Hughes Jr., Baltimore, Chemical Burns of the Eyes.
Dr. Robert Von Der Heydt, Chicago, A Clear Corneal Implant Acquires Dystrophy from Its Host.
Olof Larsell, Sc.D., Portland, Edward McCrady Jr., Ph.D., Sewanee, Tenn., and Dr. John F. Larsell, The Development of the Organ of Corti in Relation to the Inception of Hearing.
Dr. Anderson C. Hilding, Duluth, Minn., The Role of Ciliary Action in Production of Pulmonary Atelectasis and Vacuum in Sinuses.
Dr. Stuart C. Cullen, Iowa City, Anesthesia in Otolaryngology.

On Sunday a feature will be a symposium on "Seeing, Hearing, Thinking and Doing—A Problem of American Youth," presented by Drs. Joseph E. Raycroft, Princeton, N. J., Albert D. Ruedemann, Cleveland, and Albert C. Furstenberg, Ann Arbor, Mich. Sunday evening there will be the fourth annual symposium on orthoptics conducted by the American Association of Orthoptic Technicians. In addition to the scientific papers there will be a series of conference periods for members of the academy, continuance courses and a series of motion picture films.

FOREIGN

Social Security in New Zealand.—New Zealand's ambitious social security setup is costing the government only one-third the sum expected, Health Minister Arthur H. Nordmeyer, chairman of the House of Representatives committee which first endorsed the plan five years ago, declared in a review of the first four years of its operations. Before the social security plan went into gear New Zealand was paying out around $23,000,000, at current exchange rates, in yearly pensions. All these except war pensions are now a liability of the social security fund. In addition, that fund now pays out bonuses to industry under employment promotion plans, and benefits to unemployed, according to the New York *Times*. The *Times* stated that the principal field in which social security has exceeded expected costs is that in which the government was warned it would do so—the hospital field. New Zealand has the habit of putting sick soldiers into nonmilitary hospitals, which has added to the strain and helped raise costs at the expense of owners of real estate, on which local government taxes are raised to meet one third of the annual charges. Another third is met by a national government grant from general taxation, and the remaining third, or rather less, from the social security fund, it was stated. The *Times* further reported that this practice might be thought to obscure the results of the social security plan in its public health aspects. According to the report "Dr. John Cairney, medical superintendent of Wellington Hospital, stated eighteen months ago that 'even without military patients all beds and facilities would be taken up by patients on the long waiting list.' The fact is that the health plan has never operated fully since it was started owing to the shortage of doctors and hospital accommodations, and government spokesmen have admitted that wartime pressure has kept down its cost. Shortage of physicians has also kept family doctors from doing the tremendous business which was expected when medical consultation became free. Shortage of materials and labor has helped keep down hospital costs, high as these are today. Minister Nordmeyer recently told the government newspaper the *Standard* that 'during the depression many hospitals allowed building programs to fall behind, and when faced with the need for emergency accommodations for the civilian population they found themselves suddenly committed to quite extensive alterations and additions.'"

Foreign Letters

LONDON

(From Our Regular Correspondent)

Aug. 13, 1943.

Functional Diseases of the Colon and Rectum

Opening a discussion on functional diseases of the colon and rectum at the Section of Proctology of the Royal Society of Medicine, Sir Arthur Hurst said that the conditioned reflex which led to regular morning defecation might begin in the education of the infant and develop in such a way that the normal individual as he got older did not think about it at all. The most common cause of constipation, especially in women, was neglect of the normal call to defecate. If not acted on, the muscular wall of the rectum relaxed and the desire disappeared and did not return until the next quantity of feces passed into the rectum. With persistent neglect of the call the rectum became completely relaxed and distended. Well over half the cases of constipation were due not to any deficiency in the activity of the colon but to interference with the reflex. Another large group of people imagined themselves constipated when they were not. Many would report that they had a liquid stool and for years had not passed a solid one. They had been taking the aperients which figured so largely in advertisements. The symptoms of autointoxication were not produced by constipation but by the diarrhea due to the aperients taken. Another cause of upset of normal bowel activity was the procedure common some years ago and now revived: not the old fashioned Plombières douche but successive washings by one pipe after another, taking perhaps a couple of hours, in the vain expectation that eventually clear water would be returned. The procedure ignored the physiologic fact that feces were constantly coming down and mixing with the water. Mucus could be regarded as significant of a pathologic condition only if present with spontaneous diarrhea. With a loose stool caused by an aperient it was merely a protective secretion and of no importance. Mucous colitis was an imaginary complaint based on a wrong diagnosis; it was due to the idea that the presence of mucus was itself significant of disease.

The taking of aperients was the commonest cause of the low abdominal pain associated with spasm. But when such conditions as real ulcerative colitis and diverticulitis were excluded there remained a small number of cases in which colon spasm was the primary thing—a condition corresponding in some ways to asthma and not easy to diagnose or treat. He warned strongly against x-ray examination as a method of diagnosis.

Hurst finally mentioned paroxysmal proctalgia, first described as rectal crises of nontabetic origin. At intervals the patient had severe pain, always perineal, not at the anus but apparently 3 or 4 inches up the rectum. Usually it departed spontaneously after ten to fifteen minutes. It was not associated with any particular condition of the bowel but often with sexual activity. It was almost certainly due to a muscular contraction, probably at the junction of the pelvic colon and rectum. Physicians who were patients had obtained relief by having an enema syringe at their bedsides and blowing air up into the rectum.

Leprosy in the British Empire Today

At the annual meeting of the British Empire Relief Association the incidence of leprosy in Nigeria was reported to be high, the cases being estimated at over 200,000. In northern Rhodesia the work started there by certain missionary societies on lines suggested by Dr. Ernest Muir, medical secretary of the association, had been satisfactory. In a medical address Major General Sir Cuthbert Sprawson reviewed the progress made during the nineteen years since the foundation of the association. He contrasted the leprosy asylum in India then with that of today. The care of patients had greatly improved; the scientific classification of cases, their laboratory investigation and efficient treatment were now matters of routine. Patients were kept usefully employed and the atmosphere was one of hope, stimulated by the sight of many leaving the hospital fit to return to the outside world. The improvements in treatment included Rogers's introduction of active derivatives from the oil of various species of hydnocarpus seeds, better method of educating the native population in the disease and the proper mode of living for those who had contracted the disease, and increased knowledge of nutrition, malnutrition being a predisposing cause. The purely laboratory side of research on the whole yielded disappointing results, but the new leprolin and the iodide test had proved of value. More leprosy settlements and clinics were required; also separate institutions for those who had passed through the contagious stage but were too old and feeble to work. They occupied room in hospitals which was required for cases needing more urgent treatment.

Filling the Gaps in Medical Libraries After the War

In a letter to the *Times* C. C. Barnard, librarian of the London School of Hygiene and Tropical Medicine, describes the position of learned and scientific libraries as faced with the problem of attempting to fill gaps in their sets of periodicals due to the war. As stocks in European countries may also have suffered there may not be sufficient copies to go round. To prevent an unseemly scramble by the libraries for the available copies it is desirable that a representative and impartial body should decide, on a national scale, to which institutions the available copies should be allotted. This allocation should form part of a much larger scheme whereby the present holdings of learned periodicals in all libraries would be surveyed and, where necessary, redistributed in the interest of research. The obvious body to do this is the Library Association, though the actual work might be most economically done at the National Central Library. Not until this task is completed will it be possible to compile a satisfactory union catalogue of periodicals in British libraries.

Friendly Societies and the Beveridge Scheme

In previous letters the views of the medical profession have been given regarding the Beveridge scheme. As a result of what is described as a successful and profitable meeting with members of Parliament, the National Council of Friendly Societies announces the fundamentals on which it would be willing to collaborate. The following five essentials have been tabulated and are in the hands of the government ministers concerned: 1. The scheme must be susceptible of responsible administration by friendly societies. 2. It must provide for effective self government by members of the society. 3. The rates of benefits and contributions must be such as to allow a reasonable margin for voluntary insurance. 4. There must be direct contact between societies and the insured population. 5. Medical certificates must be issued free of charge to insured persons.

First Aid for Fractured Spine

Some difference of opinion has been expressed as to whether a person suspected to be suffering from fracture of the spine should be carried in the prone position. The question of first aid in such cases has been submitted to the British Orthopedic Association. After discussion at the last meeting the following opinion was given: "The executive committee decided to give authoritative support to the view that patients with suspected spinal fracture should be shifted and moved in such a way as not to be folded either backward or forward. The patient should be disturbed as little as possible, being transported as he lies. From the point of view of the spinal injury we are of the opinion that there is no indication for change of position from face to back or vice versa."

Deaths

William Fessenden Wesselhoeft, Jaffrey, N. H.; Harvard Medical School, Boston, 1887; formerly professor of clinical surgery at the Boston University School of Medicine; fellow of the American College of Surgeons and a member of the Boston Surgical Society; served in France as a lieutenant colonel and as a commanding officer of Base Hospital number 44 during World War I; introduced a new surgical knot and devised a method of sterilizing catgut that was long in use at the Massachusetts Memorial Hospitals, Boston; consulting surgeon to the Memorial Hospitals, where he at one time worked his way through the grades to the position of surgeon, and where he died, June 27, aged 81, of arteriosclerosis and chronic myocarditis.

Edward William Jones ✦ Mitchell, S. D.; Northwestern University Medical School, Chicago, 1906; past president of the South Dakota State Medical Association and the Mitchell District Medical Society; served overseas as a captain in the medical corps of the U. S. Army during World War I; coordinator of Civilian Defense and examining physician for the Selective Service Board of Davison County; on the staffs of the Methodist State and St. Joseph hospitals; for many years examining physician for the Milwaukee Railroad; treasurer of the city library board; aged 64; died, July 5, of coronary occlusion.

Harland W. Long, Mattoon, Ill.; Missouri Medical College, St. Louis, 1898; University and Bellevue Hospital Medical College, New York, 1904; member of the Illinois State Medical Society and the American Psychiatric Association; veteran of the Spanish-American and World wars; received a medal from the French government for his fight against an epidemic of influenza; formerly associated with the U. S. Veterans Bureau, Pittsburgh, and on the staff of the Veterans Administration Facility in Aspinwall, Pa.; aged 73; died, July 18, of myocardosis.

Stoddard Linnaeus Anderson, De Kalb, Ill.; Rush Medical College, Chicago, 1896; member of the Illinois State Medical Society; member of the draft board; on the staffs of the De Kalb Public and St. Mary's hospitals, De Kalb, and the Sycamore (Ill.) Municipal Hospital; aged 67; died, July 10, in Chicago of diverticulitis of the sigmoid.

Stephen Victor Balderston ✦ Evanston, Ill.; University of Pennsylvania Department of Medicine, Philadelphia, 1895; associate in medicine at the Northwestern University Medical School, Chicago; specialist certified by the American Board of Internal Medicine; served in the medical corps of the U. S. Army during World War I; health commissioner of Evanston from 1907 to 1914; for many years on the staff of the Evanston Hospital; aged 74; died, July 11, of coronary occlusion.

Mack W. Ball, New Bern, N. C.; Atlanta (Ga.) School of Medicine, 1909; aged 75; died, July 6, in the Duke Hospital, Durham, of angina pectoris.

Sydney Elon Bateman, Mifflinburg, Pa.; Medico-Chirurgical College of Philadelphia, 1904; formerly a Lutheran minister; served as a major in the medical corps of the U. S. Army during World War I; aged 79; formerly adjunct professor of histology and embryology at the Temple University School of Medicine, Philadelphia; died, July 7, in the Geisinger Memorial Hospital, Danville, of acute cholelithiasis, uremia and coronary occlusion.

Everett Charles Beach, Oxnard, Calif.; Baltimore Medical College, 1907; member of the California Medical Association; formerly supervisor of physical education in the city schools of Los Angeles and at one time director of physical education in the summer school at the University of California, Berkeley; on the staff of St. John's Hospital; aged 63; died, July 8, in the California Hospital, Los Angeles, of brain tumor.

Harold Kohli Begg ✦ Cleveland; Northwestern University Medical School, Chicago, 1918; for many years physician for the Rams and Barons, professional football and hockey teams; aged 48; died, July 13, in the Huron Road Hospital of virus pneumonia following a thyroid operation.

Theodore S. Blakesley ✦ Kansas City, Mo.; Rush Medical College, Chicago, 1902; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; served during World War I; member of the staffs of the Trinity Lutheran, St. Luke's, St. Joseph, Research and the Kansas City General hospitals; aged 65; died, July 14, in Columbus, Ohio, of coronary occlusion.

Charles James Carden, Tewksbury, Mass.; Harvard Medical School, Boston, 1896; member of the Massachusetts Medical Society; served as a major in the medical corps of the U. S. Army during World War I; formerly on the staff of the Tewksbury State Hospital and Infirmary as assistant physician; aged 70; died, July 4, of arteriosclerotic heart disease, lobar pneumonia and diabetes mellitus.

Douglas Aymar Cater ✦ East Orange, N. J.; Columbia University College of Physicians and Surgeons, New York, 1896; fellow of the American College of Surgeons; consulting physical therapist and formerly senior member of the staff of the Orange Memorial Hospital; aged 73; died, July 13, of coronary thrombosis and arteriosclerosis.

Andrew D. Clark ✦ Adrian, Mich.; Illinois Medical College, Chicago, 1910; aged 70; died, July 2, of heart disease.

R. Garn Clark, Provo, Utah; College of Physicians and Surgeons, Baltimore, 1904; member of the Utah State Medical Association; served for two years as mayor of Richfield; at one time medical director of the Richfield General Hospital; aged 66; died, July 8, in the Utah Valley Hospital of coronary occlusion.

John Hamilton Cooper, Massillon, Ohio; University of Pittsburgh School of Medicine, 1913; also a pharmacist; member of the American Academy of Ophthalmology and Otolaryngology; specialist certified by the American Board of Otolaryngology; on the staff of the Massillon State Hospital; aged 61; died, July 15.

Isham E. Cottingham, Evansville, Ind.; University of Louisville (Ky.) Medical Department, 1879; Bellevue Hospital Medical College, New York, 1881; member of the Indiana State Medical Association; aged 85; died in the Welborn-Walker Hospital, July 9, of heart disease.

William Edward Cramm, Mansfield Center, Conn.; University of Vermont College of Medicine, Burlington, 1895; served in the medical corps of the U. S. Army during World War I and as a captain in the medical reserve corps not on active duty; health officer of Mansfield for many years; a member of the visiting staff of the Windham Community Memorial Hospital, Willimantic; one of the founders and first president of the Mansfield Center Library; aged 73; died, July 7, of generalized abdominal carcinoma.

James Edward Daley, Porterville, Calif.; California Medical College, San Francisco, 1895; aged 72; died, July 3, in a San Francisco hospital of paralysis of the throat and auricular fibrillation.

Edgar Childes Dawson, Niles, Calif.; University of California Medical School, San Francisco, 1932; served on the staff of the Alameda Hospital; aged 35; died at Mount Eden, July 7, of multiple sclerosis.

Thomas J. Draper, Warrensburg, Mo.; University Medical College of Kansas City, Mo., 1894; served as public health officer of Johnson County; aged 87; formerly on the staff of the Warrensburg Clinic, where he died, July 6, of an infection of the bladder.

Austin Ray Edwards, Sidney, Ohio; Ohio State University College of Medicine, Columbus, 1916; member of the Ohio State Medical Association; served overseas during World War I; formerly coroner; on the staff of the Wilson Memorial Hospital; aged 55; died, July 10, of congestive heart disease.

Roland A. Felt, Virginia, Ill.; Barnes Medical College, St. Louis, 1899 and 1909; member of the Illinois State Medical Society; served in the medical corps of the U. S. Army during World War I; on the staffs of the Passavant Memorial and Our Saviour's hospitals, Jacksonville; aged 66; died, July 9, in St. John's Hospital, Springfield, of right pyelonephritis and urinary sepsis.

James Hudson Fiscus ✦ Greensburg, Pa.; University of Maryland School of Medicine, Baltimore, 1910; served as a captain in the medical corps of the British army during World War I; dermatologist on the staff of the Westmoreland Hospital; aged 58; died, July 4, of acute myocarditis.

Edward James Fitzgibbon, Boston; Harvard Medical School, Boston, 1904; formerly associated with the U. S. Veterans Bureau; aged 79; died in the United States Naval Hospital, Chelsea, Mass., July 12.

Tilden P. Fowler, Harrison, Ark. (licensed in Arkansas in 1903); member of the Arkansas Medical Society; aged 66; died, July 4, of cerebral hemorrhage.

Louis Morris Green, Maywood, Ill.; University of Illinois College of Medicine, Chicago, 1912; examining physician for the Baltimore and Ohio Railroad; served during World War

I; aged 62; died in the Veterans Administration Facility, Downey, July 18, of chronic myocarditis, myocardial degeneration and cerebral arteriosclerosis.

Theodore Laurence Gregg, Lewisburg, Ohio; Eclectic Medical Institute, Cincinnati, 1897; aged 68; died, July 21, in Los Angeles of cerebral hemorrhage.

Edward William Grosser, Chicago; Chicago Homeopathic Medical College, 1901; Rush Medical College, Chicago, 1902; the Hahnemann Medical College and Hospital, Chicago, 1905; aged 69; died, July 24, of chronic myocarditis and operation for carcinoma of the left kidney.

Benjamin Franklin Gumbiner, Gary, Ind.; Rush Medical College, Chicago, 1920; member of the Indiana State Medical Association; aged 47; on the staffs of St. Mary's Mercy and Methodist Hospital, where he died, July 17, of pulmonary edema.

Charles Joseph Hart ✠ New York; University and Bellevue Hospital Medical College, New York, 1921; director of the x-ray department of the Wickersham Hospital; aged 43; died in the Rutland (Vt.) Hospital, July 13, of acute dilatation of the heart following radical sinus operation.

Emil Frank Hartung, Rockville Centre, N. Y.; Long Island College Hospital, Brooklyn, 1884; at one time coroner's physician in Brooklyn; member of the draft exemption board during World War I; formerly on the staff of the Trinity Hospital, Brooklyn; aged 81; died, July 17, of senility.

Stanley Morton King ✠ Brooklyn; Albany Medical College, 1915; specialist certified by the American Board of Otolaryngology; served as a captain in the medical corps of the U. S. Army during World War I; aged 52; a member of the staffs of the New York Eye and Ear Infirmary, New York, and the Methodist Hospital, where he died, July 27, of sarcoma of the kidney.

Alfred Coleman Kinney ✠ Seaview, Wash.; Bellevue Hospital Medical College, New York, 1872; an Affiliate Fellow of the American Medical Association; member, the founder and the first and fiftieth president of the Oregon State Medical Society; one of the first members of the Oregon State Board of Health; mayor of Astoria, Ore., from 1894 to 1896; in 1938 received the honorary degree of doctor of laws from the Linfield College, McMinnville, Ore.; aged 93; died, July 13, in St. Vincent's Hospital, Portland, Ore.

LIEUT. WALTER WYTOWICH
1916-1943

Frank Ambrose Lagorio, Chicago; Northwestern University Medical School, Chicago, 1911; member of the Illinois State Medical Society; for many years chief physician of the Illinois Athletic Commission; a member of the board of the Chicago Public Library and head of the Chicago Pasteur Institute; on the staffs of the Columbus and Cuneo hospitals; aged 58; died suddenly in Winnetka, Ill., July 18, of coronary thrombosis.

Nathan Lane, Brooklyn; Columbia University College of Physicians and Surgeons, New York, 1902; member of the Medical Society of the State of New York; aged 58; died in the Harkness Pavilion of the Presbyterian Hospital, New York, July 18, of chordoma.

Robert Leroy Leighton ✠ Spring Lake, N. J.; Hahnemann Medical College and Hospital of Philadelphia, 1913; served overseas as a captain in the medical corps of the U. S. Army during World War I; member of the borough council of Spring Lake; on the staff and member of the board of governors of the Fitkin Memorial Hospital, Neptune; aged 53; died, July 5, of bronchogenic carcinoma.

Charles P. Leuthart, New Albany, Ind.; Kentucky School of Medicine, Louisville, 1901; member of the Indiana State Medical Association; for many years secretary of the Floyd County Board of Health; aged 70; died, July 16, of prostatism and myocarditis.

Gustav Edward Liebrecht, Chicago; National Medical University, Chicago, 1906; veteran of the Spanish-American War; on the staff of the Lutheran Deaconess Home and Hospital; aged 72; died, July 26, of chronic myocarditis.

Frank Ford McDede ✠ Paterson, N. J.; College of Physicians and Surgeons, Baltimore, 1901; served as a captain in the medical corps of the U. S. Army during World War I; examining physician for the Selective Service System; aged 75; on the staff of St. Joseph Hospital, where he died, July 9, of intestinal obstruction.

Stanley Willis Osgood, Clawson, Mich.; Detroit College of Medicine and Surgery, 1931; member of the Michigan State Medical Society; commissioned as a captain in the medical corps, Army of the United States, in September 1942 and relieved from active duty on account of physical disability in March 1943; served on the staffs of Mount Carmel Mercy Hospital, Detroit, and St. Joseph Mercy Hospital, Pontiac; aged 37; died, July 21, of carcinoma of the thyroid.

John Breckenridge Overall, Springfield, Ky.; Louisville Medical College, 1892; member of the Kentucky State Medical Association; served during World War I; major in the medical reserve corps not on active duty; mayor of Springfield; charter member of the Rotary Club and a member of the board of directors of the Springfield State Bank; aged 74; died, July 1, of cerebral hemorrhage.

William Gerard Paradis ✠ Crookston, Minn.; University of Minnesota Medical School, Minneapolis, 1926; past president of the Minnesota Sanatorium Association and the Red River Valley Medical Society; fellow of the American College of Chest Physicians; member of the staffs of St. Vincent's and Bethesda hospitals; medical director and superintendent of the Sunny Rest Sanatorium, where he died, July 7, of coronary thrombosis.

Thomas Francis Patterson, Brooklyn; Long Island College Hospital, Brooklyn, 1896; member of the Medical Society of the State of New York; aged 71; died, July 24.

Benjamin William Peck, Burnsville, W. Va.; Maryland Medical College, Baltimore, 1905; aged 69; died, July 8, of nephritis.

William Peters, Nicasio, Calif.; College of Physicians and Surgeons of San Francisco, 1900; formerly on the staff of the Franklin Hospital, San Francisco; aged 69; died, July 2, of heart block.

Samuel Benjamin Pond, Patton, Calif.; University of Minnesota College of Homeopathic Medicine and Surgery, Minneapolis, 1907; member of the California Medical Association and the American Psychiatric Association; on the staff of the Patton State Hospital; formerly on the staff of the Middletown (N. Y.) State Homeopathic Hospital; aged 60; died in St. Bernardine's Hospital, San Bernardino, July 20, of cerebral embolus following a prostatectomy.

Dallas Case Ragland, Los Angeles; Washington University School of Medicine, St. Louis, 1907; formerly professor of pathology and hygiene at the College of Physicians and Surgeons; aged 58; died, July 10, of cerebral hemorrhage.

Charles Henry Reinhardt, Chicago; University of Illinois College of Medicine, Chicago, 1915; served during World War I; aged 51; died, July 25, in the Wesley Memorial Hospital of carcinoma of the lung.

Hugo August John Siebeneichen, New York; University and Bellevue Hospital Medical College, New York, 1916; for many years diagnostician for the department of health; aged 49; died, July 22, of coronary occlusion.

James F. Waltz ✠ Capac, Mich.; Detroit College of Medicine, 1907; served during World War I; president of the village of Capac, 1931-1932; on the staffs of the Bishop Hospital, Almont, Harper Hospital, Detroit, and Port Huron (Mich.) Hospital; aged 57; died, June 24, of coronary occlusion.

KILLED IN ACTION

Walter Wytowich, Detroit; Wayne University College of Medicine, Detroit, 1941; served on the staff of the Grace Hospital; commissioned a first lieutenant in the medical corps of the Army of the United States in March 1942; received the Purple Heart; aged 27; was killed in action in the North African area, July 11.

Bureau of Investigation

MISBRANDED PRODUCTS

Abstracts of Notices of Judgment Issued by the Food and Drug Administration of the Federal Security Agency

[EDITORIAL NOTE.—These Notices of Judgment are issued under the Food, Drug and Cosmetic Act and in cases in which they refer to drugs and devices they are designated D. D. N. J. and foods, F. N. J. The abstracts that follow are given in the briefest possible form: (1) the name of the product, (2) the name of the manufacturer, shipper or consigner, (3) the date of shipment, (4) the composition, (5) the type of nostrum, (6) the reason for the charge of misbranding and (7) the date of issuance of the Notice of Judgment—which is considerably later than the date of the seizure of the product and somewhat later than the conclusion of the case by the Food and Drug Administration.]

Atop Nerve Tonic.—W. J. Gilmore Drug Company, Pittsburgh. Shipped between Sept. 15 and Oct. 20, 1941. Composition: essentially chloral hydrate (12 grains per fluid ounce) and sodium bromide (29 grains per fluid ounce). Misbranded for the following reasons: label lacked the warning that the product should not be taken by persons having kidney diseases and that not more than the recommended dose should be taken; absence of warning that frequent or continued use might lead to mental derangement, skin eruptions or other harmful effects; label represented that product was an appropriate treatment for nervous exhaustion and relief from symptoms of irritability, sleeplessness, headache and eye fatigue, would overcome fear and prove an efficacious treatment for the delicate mental and emotional disorders of children, prevent functional disturbances of the gastrointestinal tract, cardiac system and pelvic organs, relieve autointoxication, help correct disorders of the endocrine glands, be an appropriate treatment for the effects of alcoholic indulgence, be conducive to quick recovery from surgical shock, invaluable in anginoid cases and exceedingly helpful in other cardiac conditions and prove of value in convalescence by increasing the appetite and assisting in regaining vitality, which representations were declared false and misleading.—[*D. D. N. J., F. D. C. 610; February 1943.*]

Ayds Candy.—Shipped between May 4 and Dec. 10, 1940, by the Carlay Company, Fuller Laboratories or Fuller Company, Chicago. Misbranded because the name "Ayds," the designs of slender female figures superimposed on obese female figures and "before and after" pictures in and on the trade package falsely represented that this product and the alleged reducing "plans" accompanying it would bring about a lessening of body weight, aid the user to reduce pleasantly and without effort and enable her to keep to a desired weight once it was attained, besides helping her to cut down the amount of food eaten without feeling pangs of hunger, distress, faintness or debilitation.—[*D. D. N. J., F. D. C. 592; November 1942.*] *D. D. N. J. 593* involved the charge of misbranding brought against another lot of Ayds Candy found on sale at the Vita Health Food Company, Washington, D. C. Ayds Candy also was misbranded under the provisions of the law applicable to foods, as reported in *F. N. J. 2976 and 3625.*

Ches-O-Kol.—William A. Webster Company, Memphis, Tenn., and Ches-O-Kol Company, Spartansburg, S. C. Shipped Jan. 21, 1941. Composition: essentially camphor, menthol, eucalyptol and turpentine in a petrolatum base. Misbranded because of false and misleading label misrepresentations that the product would be effective in treating chest colds, head colds, sore throat, pneumonia, rheumatism or skin diseases, sinus trouble, hay fever, influenza and some other conditions and would penetrate and relieve congestion.—[*D. D. N. J., F. D. C. 612; February 1943.*]

Dean's Vitamin Concentrate Capsules.—Purity Drug Company, Inc., Passaic, N. J. Shipped April 18, 1941. Composition: in each capsule, not more than 800 units of vitamin D and an inconsequential amount of vitamin G (B_2), namely, approximately $\frac{1}{50}$ of the minimum daily requirement, whereas labeling declared a content per capsule of 1,000 units of vitamin D and represented that there was present a substantial amount of vitamin G (B_2). Hence adulterated and misbranded.—[*D. D. N. J., F. D. C. 627; February 1943.*] Adulterated and misbranded also under the provisions of the law applicable to foods as reported in *F. N. J. No. 3642.*

Earles Vital Vim.—W. H. Earles Company, address not given. Shipped April 25, 1941. Composition: essentially wheat germ, as labeled. Misbranded because label represented that product was efficacious in restoring and maintaining health and vigor, in preventing and treating overweight, underweight, fatigue, colitis, constipation, neuritis, arthritis, stomach disorders, indigestion, high blood pressure, hardening of the arteries and sleeplessness, in strengthening digestive organs, assisting intestinal activity and bringing about digestion and proper assimilation; in soothing the nerves; improving the circulation, toning the arteries, invigorating the heart muscles, normalizing blood pressure and warding off or preventing common colds or la grippe. These representations were declared false and misleading.—[*D. D. N. J., F. D. C. 633; February 1943.*]. Also misbranded under provisions of the law applicable to foods as reported in *F. N. J. No. 2994.*

Hoyt's Compound.—Hoyt Chemical Company, Denver. Shipped May 27, 1941. Composition: essentially water, alcohol, sugar and extracts of plant materials including a laxative. Misbranded because label did not give adequate directions for use but provided for continuous administration, whereas the product was a laxative and should not be so given. Further misbranded because substances that were not active ingredients were represented to be such on the label. Also misbranded because label represented that the product was an appropriate treatment for diseases of the stomach, bowels and kidneys, would be efficacious for rundown conditions and skin and blood diseases, and would relieve such symptoms as sour stomach, bloating, indigestion, nervousness, dizziness and muscular aches and pains.—[*D. D. N. J., F. D. C. 616; February 1943.*]

Lacto-Kelpol and Evitades.—Seal-Ins Laboratories, Inc., Los Angeles. Shipped between Aug. 15, 1940, and Jan. 4, 1941. Composition: "Lacto-Kelpol" was essentially an emulsion of mineral oil, agar agar, lactic acid (about 1 per cent) and water; "Evitades" consisted of tablets containing extracts of plant drugs. Lacto-Kelpol was misbranded because label and carton failed to give adequate directions for administration to children and because the supplementary name, "Lactic Acid Emulsion" was false, since the product owed its therapeutic action to ingredients other than lactic acid and kelp was not one of these. Also misbranded because accompanying circular falsely represented that the mixture would be of value in treating certain types of diarrhea, colitis, dysentery and constipation. Evitades was misbranded because of false and misleading statements in accompanying circular that the product was "mild in sedative action, useful in treating insomnia, also nervous disturbances of the menstrual period."—[*D. D. N. J., F. D. C. 617; February 1943.*]

Mackenzol.—R. and F. Schweickhardt, St. Louis. Shipped Jan. 16, 1941. Composition: a viscous liquid containing chiefly mineral oil and small amounts of volatile oils, including eucalyptol, thymol and methyl salicylate, with compounds of guaiacol and benzoic acid. Bacteriologic examination showed that it was not an antiseptic and hence was adulterated, especially in view of the claim "Antiseptic and Germicidal Compound." Misbranded for the same reason and because represented in labeling to be guaranteed under the Food and Drugs Act; to be antagonistic to all pathogenic organisms and to be healing; to be efficacious in the treatment of chronic laryngitis due to tuberculosis and acute and chronic nasal catarrh, especially where there was great discharge; to be of much value in the treatment of ulcerations and inflammation of the nose and throat and to possess true healing virtues after the application of an aqueous alkaline or boric acid wash or douche; to be the best antiseptic for consumption, catarrh, cough, sore throat, burns, scalds, hemorrhoids, leucorrhea, uterine infections, eczema and all disorders of the skin. These representations were declared false and misleading.—[*D. D. N. J., F. D. C. 624; February 1943.*]

Quaker Puffed Wheat Sparkies.—Quaker Oats Company, Cedar Rapids, Iowa. Shipped March 18, 1941. Misbranded because designs, devices and statements in the labeling created the false impression that this product contained vitamins A, B_1, C, D and G in consequential amounts, would be effective in preventing colds and infections, in producing healthy nerves, normal growth, good teeth, strong bones and other desirable attributes, whereas it contained no vitamin A or C and only inconsequential amounts of vitamins B_1 and G and would not be effective in producing the claimed results. Further misbranded under the provisions of the law applicable to foods.—[*D. D. N. J., F. D. C. 580; November 1942.*]

Ritamins.—American Dietaids Company, Inc., Yonkers, N. Y. Shipped between March 28 and May 13, 1941. Composition: black capsules containing vitamin A (12,800 units), vitamin B_1 (200 units), vitamin C (226 units) and vitamin D (600 units), and brown capsules containing compounds of calcium, iron, phosphorus, copper and iodine, with small amounts of compounds of other elements and an oil, such as wheat germ oil. Misbranded because labeling falsely represented that the product would supply vitamins and minerals needed for various tissues, organs and functions, whereas it did not fulfil the promises of benefits stated and implied.—[*D. D. N. J., F. D. C. 578; November 1942.*]

Rua-Balm.—Van Pelt and Brown, Inc., Richmond, Va. Shipped between Sept. 12, 1940 and Jan. 9, 1941. Composition: chiefly methyl salicylate and 14 per cent of alcohol. Adulterated because alcoholic strength was below that represented on label, which was 25 per cent. Misbranded for the same reason and because product contained two or more ingredients and label did not give the common or usual name of each. Further misbranded because label did not bear adequate warnings against unsafe methods or duration of administration for protection of users, since Rua-Balm consisted chiefly of methyl salicylate and might cause excessive irritation to the skin, particularly if applied with rubbing, and should not be permitted to get into the eyes and mucous membranes.—[*D. D. N. J., F. D. C. 609; February 1943.*]

Slend-R-Form Candy.—Riley Products, Inc., Chicago. Many shipments of different dates in 1940 and 1941. Misbranded because represented on labels to be an effective treatment for reducing body weight. Also misbranded under the provisions of the law applicable to foods, as reported in F. N. J. 2977 and 2978.—[*D. D. N. J., F. D. C. 594 and 595; November 1942.*]

Theobarb.—Van Pelt and Brown, Inc., Richmond, Va. Shipped between Sept. 12, 1940, and Jan. 9, 1941. Composition: each tablet represented to contain ¼ grain of phenobarbital, whereas it contained no more than 0.056 grain of this substance. Hence adulterated and misbranded.—[*D. D. N. J., F. D. C. 609; February 1943.*]

Virgitalis.—Van Pelt and Brown, Inc., Richmond, Va. Shipped between Sept. 12, 1940, and Jan. 9, 1941. Composition: each tablet was represented to possess an activity equivalent to that of 1½ grains of whole digitalis leaf. Adulterated and misbranded because this representation was false and misleading.—[*D. D. N. J., F. D. C. 609; February 1943.*]

Vitagen.—College Laboratories, Inc., Denver. Shipped April 22, 1941. Composition: approximately 70 per cent deficient in vitamin A and 50 per cent deficient in vitamin C, from figures claimed on label. Adulterated because valuable constituents, namely vitamins A and C, had been wholly or partly omitted or abstracted therefrom. Misbranded because statements, "two teaspoons of Vitagen contains approximately 2,810 international units of A, 450 units of C," were false and misleading when applied to an article of lower vitamin content.—[*D. D. N. J., F. D. C. 629; February 1943.*]

West Point Hair Tonic.—Associated Brands, Inc., Brooklyn. Shipped Jan. 22, 1941. Composition: essentially alcohol, water, castor oil, benzyl benzoate and benzoin. Misbranded because of false and misleading statements (on carton), "Natural Vegetable Oil Hair Tonic . . . West Point Hair Tonic wakes up tight, lazy scalps . . . and brings new life . . . to hair. . . . For Thinning Hair . . . Teach the children to use West Point Hair Tonic. It will insure their having healthy, beautiful hair when they grow older," and (on label) "Natural Vegetable Oil Hair Tonic."—[*D. D. N. J., F. D. C. 585; November 1942.*]

Zalco-Septic.—Sylvia Zalk, trading as Zalco Company, St. Paul. Shipped between Feb. 1 and Sept. 25, 1940. Composition: essentially water, alcohol and small amounts of menthol, eucalyptol, thymol, methyl salicylate and boric acid. Misbranded because when used in the dilutions recommended it was not an antiseptic for feminine hygiene.—[*D. D. N. J., F. D. C. 630; February 1943.*]

SOME MISCELLANEOUS MEDICAL FRAUDS

A Variety of Schemes Debarred from the Mails

Fraud orders issued by the Post Office Department have frequently been the subject of extensive articles by the Bureau of Investigation in these pages of THE JOURNAL. Following are brief abstracts of some fraud orders not dealt with previously:

E. J. Stevens, New Age Book and Supply House and New Age Company.—In this department of THE JOURNAL, Nov. 8, 1941, page 1642, there was reviewed the record, up to that date, of Ernest J. Stevens of San Francisco, including a Post Office fraud order issued May 17, 1941, against a long list of trade styles under which Stevens had operated. Among these were Stevens Helio-Scientific Company, The Rainbow Publishing Company, E. J. Stevens Publishing Company and The E. J. Stevens Color Institute. The article concluded with this paragraph: "As in many similar cases, the flaw in this fraud order lay in the omission of Stevens' personal name and so, like some others whose schemes have been debarred from the mails, he flouted the government and continued in business—by operating under a new trade style and local address, Chromolux Company, Stratford Hotel, San Francisco. His device also took on a new name, 'Chromolux Lamp.' His explanation to those on his mailing list was that his companies had been 'reorganized.' But this trick was soon detected by the Post Office Department, which on July 12, 1941, issued a supplemental fraud order covering not only the name of Stevens himself but also the Chromolux Company, Lux Stevens and a good many other trade styles, old and new, under which he had been operating." But Stevens is not the kind of person to let a few fraud orders or other government ukases stand in the way of his financial success, and so he simply dropped his old trade styles and adopted fresh ones, namely, "New Age Company" and "New Age Book and Supply House," and the business of promoting his "normalizer" went merrily on for a while. With it was advertised a manual entitled "True Chromo Therapy," which was represented to contain "color-energy treatments . . . for scores of diseases." This was reported by the Post Office Department to be the same manual which was involved in the earlier case against Stevens, when it was found to contain false and fraudulent claims for the treatment of disease by the Stevens devices. When it became evident to the Post Office Department that the trade styles "New Age Book and Supply House," "New Age Company" and "E. J. Stevens, M.Sc., PhD." were names under which Stevens was continuing to promote his scheme, a supplemental fraud order was issued against these titles on Feb. 15, 1943.

Holder's H. F. Condensator Company, Holder's Research Laboratories, "W. E. Holder, M.D.," "Dr. D. O. Crowe, D.M.T." and others.—These concerns and persons, whose addresses were given variously as Detroit and Windsor, Ontario, Canada, promoted through the mails a device called at different times "Holder's H. F. Condensator," "Holder's Ultra-Short Wave Condensator" and "Holder's Ultra-Short Wave H. F. Condensator." The moving spirit in the scheme was a William E. Holder, who formerly had advertised and sold through the mails a rubber chair cushion containing an electrical heating unit represented as a curative agency for a large number of serious diseases and other ailments. The operation of that scheme through the mails resulted in the issuance of a Post Office fraud order on Dec. 23, 1938, which closed the mails to Holder and others, as reported in this department of THE JOURNAL, Sept. 9, 1939, page 1051. Thereafter, it appears, Holder deemed Canada a more propitious place for his activities and set up his new enterprise in Windsor, later opening an agency in Detroit which was run by D. O. Crowe. Holder promoted his "condensator" in certain publications circulating through the mails. In one advertisement he addressed his "message to so-called incurables suffering from asthma, bronchitis, sinusitis, hay fever, colds, mastoid and throat troubles, arthritis and all rheumatic conditions, paralysis, spinal troubles, neurasthenia, stomach disorders, prostate, kidney and bladder trouble, women's weaknesses, eye ailments including cataract and glaucoma, etc., who have endeavored in vain to obtain relief." Getting down to business, his advertisement went on to say: "Such sufferers need not despair for that internationally known miracle machine, Holder's Ultra Short Wave H. F. Condensator (not diathermy) generating 'fluid' electricity with cellular massage is now being manufactured in Detroit so that United States physicians can give this wonderful treatment to aid sufferers in their recovery to 'good health.' Endorsed by the British Minister of Labor and . . . 'advertised by the British Ministry of Health as the successful treatment for colds, hay fever and sinus trouble.'" Inquirers received a printed form letter together with various so-called physicians' case-history reports, a 32-page booklet on the "condensator," and other material. The booklet contained such claims as "All bacteria-free illnesses are simply electrical unbalance. All drugs used for curative purposes must ultimately depend upon their electrical qualifications. Pain is the result of electric unbalance. Knowing these features I came to the conclusion that to balance the electrical potential in the human body it would be necessary to produce a machine which would embody the essential features necessary. . . ." The booklet went on to explain that these features were: "(1) To produce a current with immense oscillations. (2) A current which would be germicidal and have nutritional value. (3) A current of extremely high voltage. (4) A current of very low amperage. (5) A current with open circuit or spark-gap to produce a damped field of electronic-condensation. (This cannot be done otherwise.)" Also in the booklet was the promoter's claim that "the ultra short wave current which is generated in my condensator now is: of a 3 meters wave length or 100,000,000 oscillations per second, 50,000 volts intake, .2 amps, or 200 millamperes." Further, there were numerous testimonials and statements alleged to have come from physicians reporting the supposed cures of a wide variety of disorders, such as blood poisoning, paresis, infantile paralysis, cancer, including "inoperable stomach cancer," liver tumor, epilepsy, diabetes, pyorrhea, "black widow spider bite," varicose veins, cirrhosis of the liver, exophthalmic goiter, mental diseases, obesity, impotence, high blood pressure, and many others. The only condition which the literature admitted "Holder's Therapy" would not remedy was "abnormality of spine"—whatever that may be. The device sold for $365 and, though Holder contended that it was distributed only to physicians, the Post Office inspector declared that test cases that he had conducted had shown that anyone who would send the required amount would be supplied with a "condensator." On Aug. 24, 1942, the Post Office Department directed the persons and concerns in question to show cause on September 21 of that year why a fraud order should not be issued against them. At the hearing, which had been postponed to October 7, an attorney appeared for the respondents. There was produced in evidence a specimen of Holder's device, and examination showed that it consisted of a wooden cabinet about 15 inches high, about 17 inches wide and approximately 12 inches in depth. At the bottom of the cabinet was a wooden drawer in which various glass electrodes and other attachments were found. On a bakelite panel inside the top lid was a switch for turning the device on and off, with two control indicators, a socket for the insertion of the treatment attachments and a number of quarter-inch holes from which ozone emanated when the control indicator was turned to the proper mark. On the right hand side were three holes for the placing of bipolar and electrode attachments. Current was furnished to the device by connecting it with the regular electrical outlet of home or office, either alternating or direct current. Though the directions for use called for different modes of treatment for various diseases and conditions, a government witness brought out the fact that, in general, the therapy was applied locally to the area affected by the disease and elsewhere on the body. In addition to treatment by application of the electrical attachments, the ozone emanations were recommended in certain conditions. Dietary instructions were furnished and the use of food cooked in aluminum ware was prohibited. A qualified electrical and radio engineer who had spent many years in examining electrical devices testified for the government that in going over the "condensator" he had employed the best scientific instruments and followed well recognized testing procedures and that, though this device was represented in the advertising to produce "100,000,000 oscillations per second," the examination at the National Bureau of Standards showed that it actually produced not more than 250,000 oscillations or kilocycles. A qualified physician specializing in physical therapy testified for the government that the use of the "condensator" would not cure "so-called incurables" suffering from any of the numerous disorders listed in the advertising and that even if heat is indicated in the treatment of any of these, the amount of heat given off by the "condensator" would not penetrate deeply enough to produce any significant results. He testified further that some of the diseases in question require surgery, x-ray and other types of therapy for their proper treatment. It was brought out also that William E. Holder, originator and principal promoter of the device, is not a physician, had never attended any electrical school and has no scientific or college education of any sort, and that in treating persons at his residence in Windsor, Ontario, he takes at face value their statements about their physical condition; that he has had no qualified physicians associated with him; was deported from Chicago to Canada several years ago by the emigration authorities because of his promotion of the electric rubber chair cushion scheme previously mentioned, and at present is barred from returning to the United States. He is a British subject born in England in 1868. Because of his latest mail order enterprise, which the government charged was a scheme to swindle the public, a fraud order was issued Dec. 22, 1942, against him, D. O. Crowe and other names under which their operations were conducted.

Correspondence

REMOVAL OF TESTES IN TREATMENT OF MELANOMA

To the Editor:—The clinical note "Malignant Melanoma of the Choroid with Extensive Metastasis Treated by Removing Secreting Tissue of the Testicles," by William P. Herbst, published in The Journal, June 26, assumes that removal of the testes for melanoma may be followed by temporary clinical improvement as shown by the progress of the case reported following orchiectomy.

The following summary represents an example in which removal of the testes had no clinical effect in delaying the rapid downhill progress in a similar instance of widespread melanoma:

E. W., a white man aged 47, admitted to the clinic of the Brooklyn Cancer Institute on Jan. 19, 1942, first noticed a small black spot at the inner angle of his eye eight years before. Up to five years before there was hardly any noticeable increase in its size. In the last year "this black spot" had grown into a fleshy tumor mass.

A coal black papilloma measuring 0.5 by 1 by 1 cm., arising from the conjunctival surface of the lower lid, filled the inner canthus of his left eye. The patient was in good general health without evidence of metastases. His liver was not enlarged.

A radical exenteration of the orbit was recommended. This was done in another institution on Jan. 30, 1942. The pathologic diagnosis was melanoma of caruncle and conjunctiva. By February 20 most of the skin grafts had taken and the patient was discharged.

For about one year, or until February 1943, he was followed through the clinic of the Brooklyn Cancer Institute without evidence of disease. In February a subcutaneous, button-like node was felt in the anterior abdominal wall. This was excised and shown to be a metastatic melanoma. Soon after, bluish black nodules developed on the roof of the orbit and numerous discrete, subcutaneous metastases were found scattered over most of his body. His liver enlarged rapidly; ascites accumulated. It was at this time that members of the staff of the Brooklyn Cancer Institute decided to remove his testicles with the hope that the removal of the testicular male hormone might in some way impede the rapid growth and spread of these metastatic lesions.

A bilateral orchiectomy was done on April 26. There was no postoperative reaction. The patient, however, showed no evidence of clinical improvement. His downhill course was rapid and he died on June 24, 1943.

An autopsy was obtained. The following is a summary of the anatomicopathologic diagnosis: melanoma arising in conjunctiva of left eye (exenteration left orbit); metastasis of the orbital roof; metastases to skin, both lungs, hilar glands, pleurae; pleural effusion, right; metastases to pericardium, myocardium; metastases to spleen, liver, kidney, mesentery, peritoneum, omentum; ascites. There was nothing in the gross or microscopic study to suggest that the orchiectomy had in any way affected the progress of his disease.

So far the only inferences which link melanoma to the sex glands arise from the following facts:

1. With adolescence there is a localized deposition of pigment in the skin of the genitals and about the areola of the breasts.

2. Pigmented nevi which remain quiescent during infancy and childhood have been known to become activated during adolescence or later in life. The only reported case of a baby dying of malignant melanoma is that of Parkes Weber (Spontaneous Inoculation of Melanotic Sarcoma from Mother to Fetus, *Brit. M. J.* **1**:537 [March 22] 1930), who described a case of melanoma transmitted from mother to child via the placenta with death of both.

The brilliant research of Huggins, Stevens and Hodges (Studies on Prostatic Cancer: II. The Effects of Castration on Advanced Carcinoma of the Prostate Gland, *Arch. Surg.* **43**:209 [Aug.] 1941), which led up to the removal of the testes and the use of diethylstilbestrol in carcinoma of the prostate, and the work of Schinzinger (Carcinoma Mammae, *Verhandl. d. deutsch. Gesellsch. f. Chir.* **18**:28, 1889), and Beatson (On the Treatment of Inoperable Cases of Carcinoma of the Mamma: Suggestions for a New Method of Treatment, with Illustrative Cases, *Lancet* **2**:104, 162, 1896), who first demonstrated the efficacy of castration for temporary alleviation of widespread metastases in mammary carcinoma, have no counterpart in any work done on melanoma.

It is therefore suggested that great caution be exercised and a great deal more basic research be done before the testes be removed as a routine measure in the treatment of melanoma.

William E. Howes, M.D., Brooklyn.

ELECTROCARDIOGRAPHIC CHANGES IN HEART WOUNDS

To the Editor:—In The Journal, July 3, page 664, Dr. Mandel Weinstein reported a case of stab wound of the heart. In the interpretation of the electrocardiograms, he stated: "Our patient's records show the typical progression of changes seen in infarction on the anterior wall of the heart." Inspection of the electrocardiograms, however, reveals patterns which are quite typical not of infarction but rather of acute pericarditis, which, of course, is always present in any case in which an operation on the heart is performed. In other reported cases, as in this case, when a coronary artery is not ligated or involved by the wound, the electrocardiographic changes due to the wound are frequently obscured by those of pericarditis. When a coronary artery is injured or ligated, one then sees either a combined pattern of infarction and pericarditis or, occasionally, the pattern of infarction alone. In the latter cases the changes due to pericarditis are masked or neutralized by those due to the infarction. Dr. Arlie R. Barnes and I (*Arch. Int. Med.* **65**:291 [Feb.] 1940) briefly summarized the literature on the electrocardiographic changes reported in heart wounds and the reader is referred to this article for further details.

The electrocardiogram of pericarditis has been recognized only relatively recently. While it simulates that of myocardial infarction, there are a number of points of difference which enable one to make the correct diagnosis. The importance of this differentiation is obvious.

Paul H. Noth, M.D., Detroit.
Associate Professor of Medicine, Wayne University College of Medicine.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

NATIONAL BOARD OF MEDICAL EXAMINERS EXAMINING BOARDS IN SPECIALTIES

Examinations of the National Board of Medical Examiners and Examining Boards in Specialties were published in THE JOURNAL, Sept. 25, page 225.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: Montgomery, June 20-22. Sec., Dr. B. F. Austin, 519 Dexter Ave., Montgomery.

ARKANSAS: * *Medical.* Nov. 3-4. Sec., Dr. D. L. Owens, Harrison. *Eclectic.* Little Rock, Nov. 4. Sec., C. H. Young, 1415 Main St., Little Rock.

CALIFORNIA: *Written.* Sacramento, Oct. 18-21. Sec., Dr. Frederick N. Scatena, 1020 N Street, Sacramento.

CONNECTICUT: * *Written.* Hartford, Nov. 9-10. *Endorsement.* New Haven, Nov. 23. Sec. to the Board, Dr. Creighton Barker, 258 Church St., New Haven.

DELAWARE: *Written.* Dover, Jan. 11-13. *Endorsement.* Dover, Jan. 18. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniel, 229 S. State St., Dover.

DISTRICT OF COLUMBIA: * Washington, Nov. 8-9. Sec., Commission on Licensure, Dr. G. C. Ruhland, 6150 E. Municipal Bldg., Washington.

FLORIDA: * Jacksonville, Nov. 22-23. Sec., Dr. William M. Rowlett, Box 786, Tampa.

GEORGIA: October or November. Sec., State Examining Boards, Mr. R. C. Coleman, 111 State Capitol, Atlanta.

IDAHO: Boise, Jan. 11. Dir., Bureau of Occupational Licenses, Mrs. Lela D. Painter, 355 State Capitol Bldg., Boise.

ILLINOIS: Chicago, Oct. 12-14. Superintendent of Registration, Department of Registration and Education, Mr. Philip M. Harman, Springfield.

IOWA: * Iowa City, Dec. 27-29. Dir., Division of Licensure and Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines.

KANSAS: Kansas City, Feb. 2-3. Sec., Dr. J. F. Hassig, 905 N. Seventh St., Kansas City.

KENTUCKY: Louisville, Dec. 6-8. Sec., Dr. Philip E. Blackerby, 620 S. Third St., Louisville.

MAINE: Portland, Nov. 9-10. Sec., Dr. Adam P. Leighton, 192 State St., Portland.

MARYLAND: *Medical.* Baltimore, Dec. 14-17. Sec., Dr. J. T. O'Mara, 1215 Cathedral St., Baltimore. *Homeopathic.* Baltimore, Dec. 14-15. Sec., Dr. J. A. Evans, 612 W. 40th St., Baltimore.

MASSACHUSETTS: Boston, Nov. 16-19. Sec., Board of Registration in Medicine, Dr. H. Q. Gallupe, 413-F State House, Boston.

MICHIGAN: * Ann Arbor, Oct. 13-15. Sec., Board of Registration in Medicine, Dr. J. Earl McIntyre, 100 W. Allegan St., Lansing.

MINNESOTA: * Minneapolis, Oct. 19-21. Sec., Dr. J. F. DuBois, 230 Lowry Medical Arts Bldg., St. Paul.

MISSOURI: St. Louis, Nov. 15-17. Sec., State Board of Health, Dr. James Stewart, State Capitol Bldg., Jefferson City.

NEVADA: *Endorsement.* Carson City, Nov. 1. Sec., Dr. G. H. Ross, 215 Carson St., Carson City.

NEW JERSEY: Trenton, Oct. 19-20. Sec., Dr. E. S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: * *Endorsement.* Santa Fe, Oct. 11-12. Sec., Dr. LeGrand Ward, 141 Palace Ave., Santa Fe.

NORTH DAKOTA: Grand Forks, Jan. 4-7. Sec., Dr. G. M. Williamson, 4½ S. Third St., Grand Forks.

OHIO: *Endorsement.* Columbus, Oct. 7. *Written.* Columbus, Dec. 4. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus.

OREGON: * *Endorsement.* Portland, Oct. 23. Exec. Sec., Miss Lorienne M. Conlee, 608 Failing Bldg., Portland.

PENNSYLVANIA: Philadelphia and Pittsburgh, January. Act. Sec., Bureau of Professional Licensing, Department of Public Instruction, Mrs. Marguerite G. Steiner, 358 Education Bldg., Harrisburg.

RHODE ISLAND: * Providence, Oct. 7-8. Chief, Division of Examiners, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

SOUTH CAROLINA: Charleston, Dec. 20-22. Sec., Dr. N. B. Heyward, 1329 Blanding St., Columbia.

SOUTH DAKOTA: * Pierre, Jan. 18-19. Dir., Medical Licensure, State Board of Health, Dr. Gilbert Cottam, Pierre.

VERMONT: Burlington, Dec. 15-17. Sec., Dr. F. J. Lawliss, Richford.

VIRGINIA: Richmond, Dec. 14-17. Sec., Dr. J. W. Preston, 30½ Franklin Road, Roanoke.

WEST VIRGINIA: Charleston, Oct. 25-27. Commissioner, Public Health Council, Dr. John E. Offner, State Capitol, Charleston.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

CONNECTICUT: Oct. 9. Address State Board of Healing Arts, 250 Church St., New Haven.

DISTRICT OF COLUMBIA: Washington, Oct. 18-19. Sec., Dr. G. C. Ruhland, 6150 E. Municipal Bldg., Washington.

FLORIDA: DeLand, Nov. 6. Sec., Dr. John F. Conn, John B. Stetson University, DeLand.

IOWA: Des Moines, Oct. 12. Dir., Division of Licensure & Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines.

NEW MEXICO: Feb. 7. Sec., Miss Pia Joerger, State Capitol, Santa Fe.

OREGON: Portland, Oct. 30. Sec., State Board of Higher Education, Mr. C. D. Byrne, University of Oregon, Eugene.

RHODE ISLAND: Providence, Nov. 17. Chief, Division of Examiners, Mr. Thomas B. Casey, 366 State Office Building, Providence.

SOUTH DAKOTA: Vermillion, December. Sec., Dr. G. M. Evans, Yankton.

TENNESSEE: Nashville and Memphis, Dec. 10-11. Sec., Dr. O. W. Hyman, 874 Union Ave., Memphis.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Hospital Association Not Exempt from Taxation as Charitable Institution if Charity or Benevolence is Limited to Members.—The Farmers' Union Hospital Association of Elk City, Okla., was incorporated under the laws of Oklahoma relating to corporations for benevolent and charitable purposes, its articles of incorporation specifically providing that it should have no capital stock and that its profits, if any, should not inure to the benefit of the individual members but should be used for charitable and benevolent purposes. The corporation undertook to render medical and hospital care both to members of the corporation and to nonmembers. Members paid a membership fee of $50 and an annual fee that varied from year to year, being an estimate of the cost of its services for the current year in the light of past experience and future expectations. In return, members received necessary hospital and medical services and care. Nonmembers could receive available services by paying the customary cost for services received, which was at a much higher rate than for members. There was no evidence of "any conscious effort to bestow" charity or benevolence on any person not connected with the organization, though some persons did receive services without cost but, according to the evidence, that was due entirely to the inability of the association to collect from them for services previously rendered them. The association generally made an annual profit and this profit was used to increase its facilities and to reduce the cost of service to its members for the following year. The association instituted proceedings to force the county excise board of Beckham County, Okla., to exempt the association's property from ad valorem taxes. It claimed it was entitled to such exemption by reason of an Oklahoma statute that exempts from taxation "All property, both real and personal, of . . . benevolent institutions . . . or societies, devoted solely to the appropriate objects of these institutions." From adverse determinations the hospital association appealed eventually to the Supreme Court of Oklahoma.

The sole question for determination here, said the Supreme Court, is whether the property of the hospital association was utilized for charitable or benevolent purposes. If so, the property is exempt from taxation. "Charitable" is defined in 14 C. J. S. p. 407 in its broader sense as comprehending all kindly inclinations which men ought to bear toward one another, irrespective of class, conditions and invidious distinctions. In 14 C. J. S., Charities, p. 411, sec. 1, "charity" is said to embrace the sense of benevolence, philanthropy and good will, and good affections which men ought to bear toward mankind. Specifically, a charity or charitable hospital is defined as one that is not maintained for gain, profit or private advantage, 14 C. J. S.,

Charities, p. 422, sec. 2e, and cases cited in the annotations, 61 C. J. 500, sec. 597 et seq. It is generally said that "The character of the institution is to be determined, not alone by the powers of the corporation as defined in its charter, but also by the manner of conducting the hospital." *Steward* v. *California Med. etc., Ass'n*, 178 Cal. 418, 176 P. 46. There is a wealth of cases, continued the court, and a variety of schemes of organizations and methods of operation, and many are held exempt and others are not. In all of them there is one factor the presence or absence of which means almost more than anything else in determining the issue. That is this: Are the doors of the hospital open to all, poor patients and pay patients alike? If the answer is yes, it is a charitable hospital and its property is entitled to the exemption from taxation provided; if the answer is no, it is not a charitable hospital and is not entitled to the exemption. In this instance the hospital association intended charity and benevolence and private benefit and advantage to its membership and to no one else. Whatever service it dispensed for which it received no pay was accidental or incidental. Its officers very carefully refrained from saying that its doors were open to the world irrespective of ability to pay. In speaking of private advantage as being a factor that precludes any organization from assuming the status of a charitable or benevolent institution, we mean private advantage to the organizers and the supporters thereof. The fact that a profit is realized from the operation of a hospital does not condemn the scheme as noncharitable or nonbenevolent. It is the use to which the profit is put that means much. In this case some of the profit is used to increase the facilities and some to the reduction of the cost to the members. This is a private advantage. The members of the hospital association here involved cooperated for their mutual advantage, but the record is bare of any evidence of an intent on their part to distribute charity or benevolence to any person not a member.

Accordingly, the hospital property was held to be subject to taxation.—*In re Farmers' Union Hospital Ass'n of Elk City, 126 P. (2d) 244 (Okla., 1942).*

Medical Practice Acts: The Prescribing of Foods Based on a Diagnosis of Ailments Constitutes the Practice of Medicine.—Pinkus, who holds college degrees and, in the words of the court, has studied "food chemistry and science, biology and physiology," conducted a store in Newark, N. J., wherein food products were sold. On occasion, at least, he advised customers concerning their physical ailments and sold them certain "trade-name packaged" food products for the relief thereof. He was prosecuted for practicing medicine without a license in violation of the New Jersey medical practice act. At the trial, one witness testified that she told Pinkus that she had distress in her stomach and pressure around her heart and that he informed her that her condition was due to improper foods and that she should avoid starches and meats and eat "plenty of fruits and vegetables." He recommended and sold her a package of a product labeled "Sorbex." This witness testified that on another occasion she told Pinkus that she had a pain under both ears and down the side of her neck and that he informed her that her glands were not functioning properly and that she needed iron. He sold her a package of "Seatabs" and advised her to take one to four tablets daily. Later this same witness, so she testified, again visited Pinkus, informing him that she had an irritation around the waistline and had an itch. He told her that she had an acid condition, that she should not use any common table salt and that she should eat "lots of fruit, vegetables and lemons." He then sold her a package of "Vegebroth," advising her to use it twice a day. Two other witnesses testified to similar incidents and advice on the occasion of visits to Pinkus's store. Pinkus was found guilty of violating the medical practice act and prosecuted a writ of certiorari in the supreme court of New Jersey.

He contended that there was no evidence before the trial court of any violation of the medical practice act, that is, that his acts did not amount to the practice of medicine and surgery as defined in the medical practice act. The practice of medicine, said the supreme court, is defined in the medical practice act as follows:

> "Any person shall be regarded as practicing medicine and surgery, within the meaning of this chapter, who . . . holds himself out as being able to diagnose, treat, operate or prescribe for any human disease, pain, injury, deformity or physical condition, or who shall either offer or undertake by any means or methods to diagnose, treat, operate or prescribe for any human disease, pain, injury, deformity or physical condition."—R. S. **45**: 9-18, N. J. S. A. **45**: 9-18.

In view of this language, we think it is clear that the acts of Pinkus did constitute the practice of medicine. Whether or not the substances he sold and prescribed are to be classed as medicines or not makes no difference. Clearly he attempted to diagnose the "physical condition" of the witnesses and to ascribe a cause for its existence and prescribe for such condition. Pinkus argued that he was merely engaged in the sale of food and food products because he had special knowledge concerning food. But, said the court, he went far beyond the mere sale of food when he diagnosed alleged ailments of the witnesses and expressed an opinion as to their cause. We think the practices engaged in by Pinkus came within the inhibition of the act.

Pinkus next contended that the section of the medical practice act defining the practice of medicine is unconstitutional in that it is unreasonable. The power of the legislature, answered the court, to regulate the practice of medicine has been upheld many times. The contention is now made that the language of the definition is so broad that it would prohibit the mere casual suggestion by one person to another of treatment that would help a condition described. However that may be, it is not being enforced in this case in any such set of circumstances. Here Pinkus was engaged in a commercial enterprise. He sold certain products and in connection with their sale attempted to diagnose ailments and conditions and to give advice as to dieting. We think there is nothing unreasonable in prohibiting this practice by other than licensed physicians.

The judgment of conviction was in effect affirmed.—*Pinkus v. MacMahon, Judge, 29 A. (2d) 885 (N. J., 1943).*

Society Proceedings

COMING MEETINGS

American Academy of Ophthalmology and Otolaryngology, Chicago, Oct. 10-13. Dr. W. L. Benedict, 102 Second Ave. S.W., Rochester, Minn., Secretary.

American Public Health Association, New York, Oct. 12-14. Dr. Reginald M. Atwater, 1790 Broadway, New York, Executive Secretary.

Association of Military Surgeons of the United States, Philadelphia, Oct. 21-23. Colonel James M. Phalen, Army Medical Museum, Washington, D. C., Secretary.

Delaware, Medical Society of, Wilmington, Oct. 12-13. Dr. W. O. La Motte, 601 Delaware Ave., Wilmington, Secretary.

Inter-State Postgraduate Medical Association of North America, Chicago, Oct. 26-29. Dr. Arthur G. Sullivan, 16 North Carroll St., Madison, Wis., Managing Director.

Kansas City Southwest Clinical Society, Kansas City, Mo., Oct. 4-6. Dr. William M. Korth, 1115 Grand Ave., Kansas City, Mo., Secretary.

Kentucky State Medical Association, Louisville, Oct. 4-6. Dr. P. E. Blackerby, 620 South Third St., Louisville, Acting Secretary.

Oklahoma City Clinical Society, Oklahoma City, Oct. 18-21. Dr. Clark H. Hall, 117 North Broadway, Oklahoma City, Secretary.

Omaha Mid-West Clinical Society, Omaha, Oct. 25-29. Dr. J. D. McCarthy, 1036 Medical Arts Bldg., Omaha, Secretary.

Pennsylvania, Medical Society of the State of, Philadelphia, Oct. 5-7. Dr. Walter F. Donaldson, 500 Penn Ave., Pittsburgh, Secretary.

Southern Medical Association, Cincinnati, November 16-18. Mr. C. P. Loranz, Empire Building, Birmingham, Alabama, Secretary.

Virginia, Medical Society of, Roanoke, Oct. 25-27. Miss Agnes V. Edwards, 1200 East Clay St., Richmond, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1933 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Heart Journal, St. Louis

26:1-146 (July) 1943

Schneider Index as Modified by Diseases of Circulation. H. Feil, M. Petti and O. Park.—p. 1.
Blood Pressure in the Aged: Study of 1,000 Elderly Male Subjects. H. I. Russek.—p. 11.
Combined Use of Strophanthin-K and Digitalis in Treatment of Congestive Heart Failure: Preliminary Report. J. E. Garcia and B. A. Goldman.—p. 20.
Aortic Regurgitation Caused by Dilatation of Aortic Orifice and Associated with Characteristic Valvular Lesion. B. A. Gouley and E. M. Sickel.—p. 24.
Routine Use of Cedilanid in Clinical Practice. A. E. Parsonnet and A. Bernstein.—p. 39.
Electrical Conductivity of Tissues Near Heart and Its Bearing on Distribution of Cardiac Action Currents. W. Kaufman and F. D. Johnston.—p. 42.
Short PR Interval with Prolonged QRS Complex: Allergic Manifestations and Unusual Electrocardiographic Abnormalities: Report of Case. A. H. Clagett Jr.—p. 55.
Peripheral Blood Flow Under Basal Conditions in Normal Male Subjects in Third Decade. H. J. Stewart and W. F. Evans.—p. 67.
Effect of Smoking Cigarets on Peripheral Blood Flow. W. F. Evans and H. J. Stewart.—p. 78.
*Course of Blood Pressure Before, During and After Coronary Occlusion. A. M. Master, H. L. Jaffe, S. Dack and N. Silver.—p. 92.
Duration of Ventricular Systole as Measured by QT Interval of Electrocardiogram, with Especial Reference to Cardiac Enlargement With and Without Congestive Failure. S. H. Phang and P. D. White.—p. 108.
Depressor Effect of Tissue Implants in Hypertensive Dogs. S. Rodbard and L. N. Katz.—p. 114.

Blood Pressure and Coronary Occlusion.—Master and his co-workers investigated the blood pressure in 538 attacks of coronary occlusion. Slightly over half of the attacks were initial ones and the remainder were second or third attacks. The authors employed the following criteria in judging whether hypertension had been present before the attacks: (1) a systolic pressure of 150 mm. or more at any time during observation, (2) a diastolic pressure of 96 mm. or more prior to the attack, (3) a diastolic pressure of 90 mm. or more during or after the attack and (4) pronounced enlargement of the heart without obvious cause. It was found that the incidence of hypertension increased with age. The blood pressure fell in every case, but in a few the fall was slight. A transitory rise in pressure occurred infrequently at the onset of the attack. A rapid fall was somewhat more common than a gradual one. Occasionally the fall did not occur until after a week. The lowest pressure was usually reached between the twelfth and twentieth days. In some cases the initial fall was soon followed by a temporary or permanent rise in pressure. The trend of the blood pressure was similar in the hypertensive and nonhypertensive groups, although a rapid fall was more common among the nonhypertensive patients who died. The systolic blood pressure rarely fell below 90 mm. in the hypertensive group, but this was common in the nonhypertensive group. When the pressure fell below 80 the patient usually died. In almost one fifth of the patients with a previous pressure of 200 mm. or more the pressure did not fall below 150 mm. Two thirds of the hypertensive patients regained a hypertensive level; in half of these this took place before discharge from the hospital, and in the remaining half usually within one or two years. The height of the blood pressure after the attack did not significantly influence the future course of the case with respect to subsequent angina pectoris, heart failure, coronary occlusion or death.

American Journal of Clinical Pathology, Baltimore

13:285-328 (June) 1943

Idiopathic Hypoprothrombinemia. A. S. Giordano.—p. 285.
Blood Amylase. D. Polowe.—p. 288.
Diastase Content of Blood and Urine in Acute Alcoholism. H. Siegel and B. Krautman.—p. 302.
Postmortem Examination in Cases of Suspected Rape. O. J. Pollak.—p. 309.
Transfusion Reaction Caused by Proven Dangerous Universal Donor. S. Weintraub.—p. 315.
Agranulocytosis Following Use of Novaldin: Report of Case. W. Moloney and M. Vidoli.—p. 317.
*Thallium Poisoning: I. Detection of Thallium in Biologic Material. A. O. Gettler and L. Weiss.—p. 322.

Thallium Poisoning.—Gettler and Weiss state that, before proceeding to the actual detection of thallium, all organic matter in the tissue must be destroyed by an oxidative process. They list the procedures for the digestion of biologic material and describe the method which they found to be least time consuming and at the same time yielding a solution free of all organic substances. The various qualitative tests for thallium are critically reviewed. A detailed description for the detection of thallium in biologic material is given.

American J. Obstetrics and Gynecology, St. Louis

46:1-46 (July) 1943. **Partial Index**

Infantile Mortality and Bacteriologic Investigations of Effect of Prolonged Labor on Baby. R. G. Douglas and H. J. Stander.—p. 1.
*Further Contribution to Syndrome of Fibroma of Ovary with Fluid in the Abdomen and Chest, Meigs's Syndrome. J. V. Meigs, S. H. Armstrong and H. H. Hamilton.—p. 19.
*Nutrition Studies During Pregnancy. Bertha S. Burke, Virginia A. Beal, S. B. Kirkwood and H. C. Stuart.—p. 38.
Detection of Ovulation by Basal Temperature Curve with Correlating Endometrial Studies. P. L. Martin.—p. 53.
Rate of Filtration Through Capillary Walls in Pregnancy. C. E. McLennan.—p. 63.
Report on Sequential Abortion. E. Allen.—p. 70.
Fluidity of Menstrual Blood, a Proteolytic Effect. C. Huggins, Virginia C. Vail and M. E. Davis.—p. 78.
Hypothyroidism as a Problem in Women: Second Report. C. H Davis.—p. 85.
Attempt to Correlate Preeclamptic State with Congenital Anomaly of Kidney. R. M. Humter.—p. 91.
Favorable Response of Advanced Endometriosis to Testosterone Propionate Therapy. J. C. Hurst.—p. 97.
Combined X-Ray and External Pelvimetry. D. J. McSweeney and A. M. Moloney.—p. 102.
Relation of Sacral Promontory to Pelvic Inlet. H. Thoms.—p. 110.
Effect of Complementing Diet in Pregnancy with Calcium, Phosphorus, Iron and Vitamins A and D. F. L. Adair, W. J. Dieckmann, H. Michel and others.—p. 116.

Meigs's Syndrome.—Meigs and Cass reported in 1937 4 cases of ascites and hydrothorax associated with fibroma of the ovary. The serous effusions disappeared with removal of the tumor. In the years following the first presentation of this syndrome other cases were reported and brought to the authors' attention. The present report by Meigs, Armstrong and Hamilton lists 27 authentic cases. The syndrome is of considerable importance, for some patients have died without proper surgical relief while others, doomed because of a tumor considered inoperable, are now well. Two patients operated on in 1941 presented an opportunity to palpate the structure of the diaphragm and to collect fluid for investigation. The fluid in the abdomen and that in the chest were identical. Particulate carbon passed from the abdominal to the thoracic fluid quickly and easily. Three important investigative problems emerge from Meigs's syndrome: (*a*) the mechanism whereby ovarian fibroma gives rise to abdominal fluid, (*b*) the mechanism of the hydrothorax, (*c*) the question of whether similar mechanisms operate in combined hydrothorax and ascites when the primary pathologic condition is other than fibroma of the ovary. Cullen, Kelly and others showed that fluid may be present in the abdomen with lesions other than ovarian fibroma. That this fluid is similar to the fluid found with fibroma has not been proved, though it may be considered probable. In most cases of uterine fibroid with fluid there are adhesions of omentum to the tumor or twists of the pedicle, which were not present in the cases reported here. It remains for joint investigation by thoracic surgeons and others to demonstrate the presence of diaphragmatic perforations of small or large size or the presence of the rarely reported pleuroperitoneal tubes

and to determine the direction and the degree of penetrability of the diaphragmatic lymphatics. The syndrome of ovarian fibroma with hydrothorax and ascites is of practical clinical significance.

Studies of Nutrition During Pregnancy.—Burke and her associates studied 216 women chosen from the antepartum clinics of the Boston Lying-in Hospital. These women were seen at least monthly through the seventh month of pregnancy, every two weeks during the eighth month and weekly thereafter unless more frequently because of complications. The study revealed a relationship between the diet of the mother during pregnancy and the condition of her infant at birth. All stillborn infants, all infants who died within a few days of birth with the exception of one, the majority of infants with well defined congenital defects, all premature infants and all "functionally immature" infants were born to mothers whose diets during pregnancy were very inadequate. If the mother's diet during pregnancy is excellent or good her infant will probably be in excellent or good physical condition. There was one exception to this in the present series of cases. A statistically significant relationship was found between the antepartum diet and the course of pregnancy. This relationship, however, was not as clear as that between the antepartum dietary rating and the condition of the infant. This indicates that when nutrition during pregnancy is inadequate the fetus suffers to a greater degree than the mother. In this study no mother whose diet during pregnancy was considered "good" or "excellent" had preeclampsia, while with a "poor to very poor" diet during pregnancy almost 50 per cent had preeclampsia. No statistically significant associations were found between antepartum nutrition and the duration or the character of labor and delivery. There was a tendency for the mothers whose diets during pregnancy were "poor to very poor" to have more difficult types of labor and to have more major complications at delivery despite the fact that these women had on the average smaller infants than were born to the women whose diets were "good" or "excellent." No relationships of statistical significance were found between antepartum nutrition and the postpartum course. There seemed to be a tendency toward a relationship between antepartum nutrition and the occurrence of major complications in the puerperium.

American Journal of Surgery, New York

61:1-156 (July) 1943

*Perinephric Abscess in Infants and Children: Study of 26 Patients Surgically Treated. H. Swan.—p. 3.
Present Status of Gastric and Duodenal Ulcer. J. L. DeCourcy.—p. 11.
Pentothal Sodium Oxygen Anesthesia in Major Surgery. E. A. French.—p. 16.
Acute Cholecystitis: Certain Pathologic and Surgical Aspects. G. T. Root and J. T. Priestley.—p. 38.
Five Years' Experience with Hemo-Irradiation According to Knott Technic. H. A. Barrett.—p. 42.
Phlegmonous Cecitis: Report of 2 Cases and Review of Literature. A. H. Spivack and I. Busch.—p. 54.
Operation for Pilonidal Sinus. I. Cohn.—p. 61.
Traumatic Rupture of Spleen: Experiences with 10 Cases in General Hospital. H. N. Harkins and E. J. Zabinski.—p. 67.
Diagnosis of Perforated Ulcer: Two Useful Maneuvers by Means of Which Pneumoperitoneum and Diaphragmatic Irritation are Demonstrated More Clearly. A. E. Pearce.—p. 76.
Theory and Therapy of Shock: Excessive Fluid Administration. F. M. Allen.—p. 79.
Improved Technic for Blind Nailing of Neck of Femur: Crecca-Cetrulo Guide. W. D. Crecca and G. I. Cetrulo.—p. 93.
Sulfadiazine Anuria: Its Relief by Ureteropyelostomy. M. F. Campbell and J. H. Fobes.—p. 99.
Technic for Repair of "Baseball" Finger. G. M. Saypol.—p. 103.
Skin Grafting: New Method Based on Principles of Tissue Culture. M. E. Sano.—p. 105.

Perinephric Abscess in Infants and Children.—Swan stresses that perinephric abscess is not as rare in infants and children as is generally believed. He reviews a series of 26 proved and 6 possible cases. It is important for prognostic and therapeutic reasons to classify patients on the etiologic basis of their lesion as metastatic, complicated by underlying renal disease or secondary to trauma to the kidney. In children a history which includes urinary complaints or a finding of albumin or white cells in the urine strongly suggests a complicated type of lesion and indicates a thorough study of the urinary tract. An intravenous pyelogram should be done preoperatively on all patients suspected of having a perinephric abscess unless they are too ill to tolerate the procedure. Early incision and drainage is the treatment for metastatic or traumatic abscess. In abscess complicating urinary disease, therapy must be individualized and is twofold in purpose: (1) the immediate treatment of the abscess and (2) the subsequent treatment of the underlying urinary tract disease. The mortality was nil and the hospitalization averaged about three weeks in children with metastatic or traumatic abscess. The mortality was 45 per cent and the hospital stay averaged ten weeks in children in whom abscess complicated urinary disease.

American Journal of Tropical Medicine, Baltimore

23:309-380 (May) 1943

Infectivity of Texas Strain of Trypanosoma Cruzi to Man. A. Packchanian.—p. 309.
Observations on Vectors of Chagas' Disease in United States: II. Arizona. S. F. Wood.—p. 315.
Employment of Rickettsial Vaccine for Antigen in Diagnostic Complement Fixation Test. F. H. K. Reynolds and M. Pollard.—p. 321.
Amebic Infection of Vagina and Uterus. Esther M. Morse and S. P. Seaton.—p. 325.
Incidence of Amebiasis Observed at Chicago Hospital over Twelve Year Period. M. Hood.—p. 327.
Multiple Deficiency Disease with Allergy and Nutritional Enteritis: Case Report. A. C. Reed, J. L. Carr and F. Rochex.—p. 333.
Death Due to Akee Poisoning in Panama. B. H. Kean.—p. 339.
Comparison of Three Strains of Trichinella Spiralis: I. Pathogenicity and Extent of Larval Development in Musculature. I. Rappaport.—p. 343.
Id.: II. Longevity and Sex Ratio of Adults in Intestine and Rapidity of Larval Development in Musculature. I. Rappaport.—p. 351.
Diphyllobothrium Latum in Florida. W. A. Summers and P. P. Weinstein.—p. 363.
Factors Influencing Reported Incidence of Appendical Oxyuriasis. L. E. Rector.—p. 369.
Report Concerning Certain Anophelines Found Near Mexican Guatemalan Frontier. H. W. Kumm, M. E. Bustamante and J. R. Herrera.—p. 373.
Clinical Use of Flea Antigen in Patients Hypersensitive to Flea Bites. Barbara C. McIvor and L. S. Cherney.—p. 377.

Archives of Neurology and Psychiatry, Chicago

50:1-110 (July) 1943

Intramedullary Cavitation Resulting from Adhesive Spinal Arachnoiditis. J. Nelson.—p. 1.
Effect of Metrazol Convulsions on Conditioned Reflexes in Dogs. V. H. Rosen and W. H. Gantt.—p. 8.
Clinical and Electroencephalographic Studies on Criminal Psychopaths. D. Silverman.—p. 18.
Integrated Facial Patterns Elicited by Stimulation of Brain Stem. E. A. Weinstein and M. B. Bender.—p. 34.
Primary Sarcomas of Brain: Review of Literature and Report of 12 Cases. K. H. Abbott and J. W. Kernohan.—p. 43.
Dermatome Hypalgesia Associated with Herniation of Intervertebral Disk. J. J. Keegan.—p. 67.

Archives of Surgery, Chicago

47:1-120 (July) 1943

Guide to Replacement Therapy for Loss of Blood or Plasma. H. P. Jenkins, P. W. Schafer and F. M. Owens Jr.—p. 1.
Ligation of Saphenous Vein for Varicose Veins. R. W. Postlethwait.—p. 4.
Sarcoma of Stomach: Clinical and Pathologic Study. G. F. Schroeder and H. J. Schattenberg.—p. 8.
Treatment of Acute Cholecystitis: Suggested Two Stage Treatment. D. MacDonald.—p. 20.
Influence of Hepatic Function on Metabolism of Vitamin A. K. A. Meyer, F. Steigmann, H. Popper and W. H. Walters.—p. 26.
Plasma Clot Suture of Nerves: Experimental Technic. I. M. Tarlov, C. Denslow, S. Swarz and D. Pineles.—p. 44.
Mechanism of Erythremia: Erythremia Resulting from Traumatic Shock in Dogs and from Injections of Epinephrine into Human Beings and Dogs. R. D. Taylor and I. H. Page.—p. 59.
Angiofibroma of Ileum: Clinical Picture in Tumors of Small Intestine. M. E. Lichtenstein and F. R. Dutra.—p. 69.
Chronic Effects Resulting from Downward Traction on Liver. W. M. Booker.—p. 76.
Review of Urologic Surgery. A. J. Scholl, F. Hinman, A. von Lichtenberg, A. B. Hepler, R. Gutierrez, G. J. Thompson, E. N. Cook, E. Wildbolz and V. J. O'Conor.—p. 86.

Bulletin New York Academy of Medicine, New York

19: 447-522 (July) 1943

Role of Kidney in Genesis of Hypertension. H. W. Smith, W. Goldring and H. Chasis.—p. 449.
Special Aspects of Problem of Renal Origin of Hypertension. I. H. Page.—p. 461.
Management of Peripheral Vascular Disease. A. W. Duryee.—p. 478.
Dietary Treatment of Laënnec's Cirrhosis with Special Reference to Early Stages of Disease. A. J. Patek Jr.—p. 498.
Present Status of Continuous Caudal Analgesia in Obstetrics. W. B. Edwards and R. A. Hingson.—p. 507.

Diseases of Chest, Chicago

9:297-382 (July-Aug.) 1943

*Sulfadiazine Pneumonia Therapy in Canal Zone (With Especial Reference to Bradycardia). S. M. Browne, H. P. Marvin and E. R. Smith.—p. 297.
Inhalation of Nebulized Solutions of Sulfonamides in Treatment of Bronchiectasis. J. W. Stacey.—p. 302.
Bronchoscopic Aids in Medical Conditions Within Chest. J. W. Peabody.—p. 307.
Correlated Applied Anatomy of Bronchial Tree and Lungs with System of Nomenclature. C. L. Jackson and J. F. Huber.—p. 319.
Post-Thoracoplasty Care: Scoliosis, Pain and Rehabilitation. R. Shaw. —p. 327.
Hexylresorcinol Solution in Treatment of Tuberculous Empyema. J. J. Mendelsohn.—p. 334.
Woodward High School Survey. Barbara A. Hewell and H. J. Nimitz.—p. 348.

Sulfadiazine Therapy of Pneumonia in Canal Zone.—Browne and his collaborators treated 100 consecutive unselected pneumonia patients in the Canal Zone with sulfadiazine. They utilized the original dosage recommended by the Council on Pharmacy and Chemistry, namely 0.10 Gm. per kilogram of body weight initially, followed by 1 Gm. every four hours day and night until a normal temperature had been present for seventy-two hours, at which time the chemotherapy was discontinued. There were 45 lobar and 55 bronchopneumonias. The average length of time between onset of symptoms and hospital admission was 4.07 days. Bacteriologically there were 42 typed pneumococcus (including 10 type I), 7 hemolytic streptococcus and 51 cases of undetermined etiology. The average sulfadiazine dosage was 40.5 Gm. The maximum sulfadiazine concentrations varied from 8 mg. to 30.8 mg. per hundred cubic centimeters. The temperature returned to normal by crisis within forty-eight hours in 78 patients, by lysis in 21 (one death). Pneumonia and drug complications with complete recovery in all cases were as follows: jaundice, 1; serous pleural exudate, 2; nausea and vomiting, 1. There was one death, a mortality rate of 1 per cent. Most noteworthy and inexplicable was the fact that 63 of the 100 patients developed a sinus bradycardia with occasional heart rates as slow as 36 beats per minute during or immediately following sulfadiazine treatment. The authors conclude that sulfadiazine is most efficacious in pneumonia, that it is equally effective in the treatment of pneumonia in tropical as well as in other climates, and that it is accompanied by fewer drug reactions than sulfapyridine or sulfathiazole.

Gastroenterology, Baltimore

1:555-634 (June) 1943

*Significance of Gastroscopic Findings in Patients with Duodenal Ulcer. H. J. Tumen and M. M. Lieberthal.—p. 555.
Allergic Reaction in Gallbladder: Experimental Studies in Rhesus Monkey. M. Walzer, I. Gray, M. Harten, S. Livingston and D. Grayzel.—p. 565.
Sulfonamide Treatment and Clinical Significance of Chronic Biliary Tract Infections. L. M. Morrison, W. A. Swalm, W. E. Burnett, F. W. Konzelmann and E. J. Spaulding.—p. 573.
In Situ *pH* of Antrum of Stomach, Pylorus and Duodenum. H. C. Breuhaus and J. B. Eyerly.—p. 583.
Effect of Thymoxyethyldiethylamine (929 F) on Gastric and Intestinal Motility; an Experimental Study. G. A. Hallenbeck, C. F. Code and F. C. Mann.—p. 588.
Study of Excretion of Cinchophen in Bile and Urine and Posology of Drug. J. H. Annegers, F. E. Snapp, A. C. Ivy, A. J. Atkinson and A. L. Berman.—p. 597.

Gastroscopic Findings in Patients with Duodenal Ulcer.—Tumen and Lieberthal made gastroscopic studies on 50 patients with duodenal ulcer uncomplicated by pyloric obstruction. Of these, 33 had chronic gastritis, 1 had unclassifiable inflammatory changes and 16 had normal stomachs. Six of the 16 patients with no evidence of gastritis had an atypical history or poor response to treatment or both. Twenty-one of the 33 patients with gastritis had an atypical history or poor response to treatment or both. While the incidence of atypical history and/or poor treatment response was somewhat greater in ulcer patients who had gastritis than in those who had not, it is difficult to ascribe much significance to this because among the 21 patients with gastritis who were examined by gastroscope more than once, the clinical severity of the symptoms seemed related to the gastroscopic picture in only 10. In the remaining 11 there was no correlation between the gastroscopic picture and the presence or character of symptoms. The presence of gastritis did not regularly influence the clinical course of duodenal ulcer. It was impossible to postulate the presence or absence of associated gastritis on the basis of the nature of the symptoms or the character of the response to treatment.

Georgia Medical Association Journal, Atlanta

32:151-184 (May) 1943

Some Urgent Needs for Medical Advancement. J. A. Redfearn.—p. 151.
Lesions of Esophagus and Stomach. W. F. Lake.—p. 154.
Diagnostic Methods Utilized in Study of Colon with Consideration of Various Types of Disease Found. J. J. Clark.—p. 156.
Chronic Appendicitis. A. A. Rayle.—p. 157.
Roentgenologic Studies of Gallbladder. J. W. Landham.—p. 161.
One Hundred and One Years of Anesthesia. J. S. Lundy.—p. 167.
Recommendations for Venereal Disease Control Program in Industry: Report of Advisory Committee on Control of Venereal Diseases. O. L. Anderson.—p. 172.

32:185-220 (June) 1943

Symposium on Eye, Ear, Nose and Throat Problems: Aneurysm in Eyelid; Report of Case. S. J. Lewis.—p. 185.
Id.: Dacryocystorhinostomy: Logical Treatment of Occlusion of Lacrimal Sac. A. V. Hallum.—p. 186.
Id.: Treatment and Care of Common Eye Injuries. W. O. Martin Jr. —p. 189.
Id.: Osteomyelitis of Frontal Bone. L. A. Brown.—p. 192.
Id.: Laryngectomy for Carcinoma. M. Equen, F. Neuffer, W. B. Matthews and F. Ogden.—p. 194.
Hirschsprung's Disease: Report of Cases. C. H. Watt.—p. 197.
Treatment of Perforated Duodenal Ulcer from Surgical Standpoint. J. C. Blalock.—p. 205.

Indiana State Medical Assn. Journal, Indianapolis

36:331-378 (July) 1943

Realistic Approach to Present Medical Problems. F. W. Rankin. —p. 331.
Prevention and Treatment of Infections of Hand. V. E. Siler.—p. 334.
Treatment of Uncomplicated Diabetes with Mixtures of Insulin and Protamine Zinc Insulin. F. B. Peck.—p. 340.
Report of Case of Palindromic Rheumatism. J. L. Ferry.—p. 348.

Journal of Clin. Endocrinology, Springfield, Ill.

3:321-388 (June) 1943

Excretion of Sex Hormones in Abnormalities of Puberty. I. T. Nathanson and J. C. Aub.—p. 321.
Gonadotropin Excretion in Normal Men and Women and Cases of Hysterectomy, Menopause, Migraine, Epilepsy and Eunuchoidism. R. Main, W. Cox, R. O'Neal and J. Stoeckel.—p. 331.
Metabolic Changes in Patient with Addison's Disease Following Onset of Diabetes Mellitus. G. W. Thorn and M. Clinton Jr.—p. 335.
Diabetes Mellitus Associated with Hirsutism and Unusual Insulin Resistance: Case Report. R. L. Pullen and W. A. Sodeman. —p. 345.
Serum Phosphatase Activity in Hyperparathyroidism. N. C. Klendshoj and G. F. Koepf.—p. 351.
*Melanotropic Hormone and Vitiligo: Report of 11 Cases. J. C. M. Fournier, J. M. Cervino and O. Conti.—p. 353.
Therapy of Seminal Inadequacy: II. Use of an Extract of Chorionic Gonadotropin and "Pituitary Synergist." C. D. Davis, J. H. M. Madden and E. C. Hamblen.—p. 357.
Breast Hypertrophy in Male: Report of 2 Cases of Pseudogynecomastia with Surgical Reconstruction. J. W. Maliniac.—p. 364.
Structure of Human Anterior Pituitary Gland After Administration of Estrogenic Hormones. C. Spark.—p. 367.

Melanotropic Hormone and Vitiligo.—The fact that the pituitary gland produces a melanotropic hormone and that dyschromia occurs in both hypopituitarism and hyperpituitarism led Fournier and his collaborators to investigate the possible effect of treatment with this hormone on vitiligo. The authors employed the hormone in 11 cases. Treatment was started by giving a local intradermal injection of 400 frog units twice a week. The beneficial effect consisted in a striking reduction in the area of the leukoderma. This therapy proved successful in 8 of 11 patients (73 per cent). One patient was given fresh bovine hypophyses orally; 9 others were given a purified extract of the hormone either locally or subcutaneously. The systemic action of these therapeutic measures is shown by the improvement in areas of vitiligo remote from the site of local intradermal injections. Local ionization with the melanotropic hormone was tried successfully once. Improvement was more rapid and was of a greater degree in the patches which had appeared recently. Satisfactory results were likewise obtained in cases of vitiligo of ten years' duration.

Journal Industrial Hygiene & Toxicology, Baltimore

25:199-140 (June) 1943

Physiologic Response of Rabbits to Cyclohexane, Methylcyclohexane and Certain Derivatives of These Compounds: I. Oral Administration and Cutaneous Application. J. F. Treon, W. E. Crutchfield Jr. and K. V. Kitzmiller.—p. 199.
*Byssinosis: Report of 2 Cases and Review of Literature. H. L. Bolen.—p. 215.
Threshold Toxicity of Gasoline Vapor. P. Drinker, C. P. Yaglou and Madeleine Field Warren.—p. 225.
Physiologic Properties of Indium and Its Compounds: II. G. C. Harrold, S. F. Meek, N. Whitman and C. P. McCord.—p. 233.
Hypersensitivity to Adhesive Tape: Report of 4 Cases Showing Its Variable Etiology. H. Keil.—p. 238.
Determination of Volatile Halogenated Hydrocarbons in Blood. H. E. Moran.—p. 243.

Byssinosis.—According to Bolen the term byssinosis is applied to a form of respiratory disease affecting workers in cotton mills, where much dust is given off in the processes of preparing the cotton for spinning and weaving. In the early stage the symptomatology is similar to the so-called heckling fever, mill fever or Monday fever affecting workers in cotton mills. The onset is insidious. The victim sneezes frequently, develops a slight, dry, increasingly irritating cough and is aware of a feeling of constriction in the chest. Dyspnea becomes more pronounced. As the fine particles or strands of cotton become lodged in the lungs an irritation is set up and the breathing becomes more labored, the cough more metallic. The disease progresses, with individual variation, over a period of years. As the cotton dust makes its way into the finer bronchi there is a decrease in vital capacity. The victim becomes a semi-invalid and is forced to give up work entirely. Before this stage of permanent disability is reached, however, many workers change their occupation. The author reviews the literature on byssinosis and presents the histories of 2 patients both of whom had worked for many years in the card room of a cotton mill. In 1936 an outbreak of respiratory disturbances among workers in a North Carolina mill called attention to the need of preventive measures to eliminate the health hazard. As reports from other mills appeared from time to time, steps were taken to control card room dust by installing vacuum strippers and grinders and ventilators. The workers are given frequent physical examinations, and those who exhibit excessive sensitivity to the cotton dust are urged to seek other employment. There is no specific treatment for byssinosis. Removal from exposure should be the first step if the worker appears to be susceptible, and then symptomatic or preventive treatment is instituted. In the late stages treatment can be at best only palliative, because irreversible structural changes have taken place in the lungs. Johnstone recommends for the treatment of dust diseases general tonics, vitamins, adequate diet, cough mixtures, mild narcotics and limited activity.

Journal of Lab. and Clinical Medicine, St. Louis

28:1053-1174 (June) 1943

Distribution and Pollination Times of Important Hay Fever Producing Plants in United States. P. M. Gottlieb and E. Urbach.—p. 1053.
Surface Films Formed by Blood Plasma and Serum of Patients with Chronic Arthritis. C. W. Scull and R. Pemberton.—p. 1070.
Vitamin A and Detoxication of Monobromobenzene. F. L. Haley and G. S. Samuelsen.—p. 1079.
Syringadenitis Suppurativa Tropicalis (Complication of Lichen Tropicus): Histologic Appearance and Etiologic Considerations Particularly as to Possible Relationship of Ascorbic Acid and Carbohydrate Metabolism. F. Reiss.—p. 1082.
Diffusion of Dyes in Ethylene Glycol Gels. Frances C. Brown and E. E. Reid.—p. 1093.
Seasonal Variations in Some Physiologic Variables. M. A. Wenger. —p. 1101.
Effect of Continued Sulfanilamide Ingestion on Acid Base Equilibrium of Dog. A. H. Free, D. E. Bowman and D. F. Davies.—p. 1109.
Protein Hydrolysate in Regeneration of Serum Protein in Hypoproteinemic Rat. D. B. Sabine and H. R. Schmidt.—p. 1117.

Journal-Lancet, Minneapolis

59:163-192 (June) 1943

Medical Management of Patient with Arterial Hypertension. S. M. White.—p. 163.
Safety in Cataract Extraction. L. G. Dunlap.—p. 170.
Health Trends in University of Michigan Women Students. Margaret Bell and Claire E. Healey.—p. 172.
Syphilis Serology in North Dakota. M. E. Koons.—p. 177.
Complaint and Situation in College Health Work. T. Raphael and L. E. Himler.—p. 182.
Variable Pulmonary Infiltration Association with Boeck's Sarcoid: Case Report. C. A. McKinlay.—p. 185.

Journal of Nat. Cancer Inst., Washington, D. C.

3:449-582 (June) 1943. Partial Index

Effect of Diet Relatively Low in Cystine on Production of Spontaneous Mammary Gland Tumors in Strain C3H Female Mice. J. White and H. B. Andervont.—p. 449.
Quantitative Experiments on Production of Subcutaneous Tumors in Strain A Mice with Marginal Doses of 3, 4-Benzpyrene. J. Leiter and M. J. Shear.—p. 455.
Degradation of Cystine by Normal Liver but Not by Transplanted Hepatomas. J. P. Greenstein.—p. 491.
Hydrogen Ion Concentration of Normal Liver and Hepatic Tumors. H. Kahler and W. v. B. Robertson.—p. 495.
Quantitative Analysis of Dose Response Data Obtained with Three Carcinogenic Hydrocarbons in Strain C3H Male Mice. W. R. Bryan and M. B. Shimkin.—p. 503.
Wavelength Dependence of Tumor Induction by Ultraviolet Radiation. H. F. Blum.—p. 533.
Neoplasms and Other Lesions of Eye Induced by Ultraviolet Radiation in Strain A Mice. S. W. Lippincott and H. F. Blum.—p. 545.
Changes Induced in Strain of Fibroblasts from Strain C3H Mouse by Action of 20-Methylcholanthrene: Preliminary Report. W. R. Earle.—p. 555.
Morphology of Sarcomas Derived from Fibroblasts Previously Treated with 20-Methylcholanthrene in Vitro: Preliminary Report. A. Nettleship.—p. 559.
Study of Spontaneous Mouse Rhabdomyosarcoma. A. Nettleship. —p. 563.

Kansas Medical Society Journal, Topeka

44:181-216 (June) 1943

Fundamentals of Psychiatry: IX. Theory of the Unconscious. W. C. Menninger.—p. 183.
Case of Pseudohermaphrodite with Exstrophic Bladder. S. L. Loewen and L. O. Rupe.—p. 186.
Rickettsias and Pathogenic Viruses: Our Present Orientation. F. A. Carmichael.—p. 189.

44:217-252 (July) 1943

State Procurement and Assignment. F. H. Lahey.—p. 217.
Procurement and Assignment Service for Physicians, Dentists and Veterinarians—Responsibilities, Accomplishments and Future Problems. H. S. Diehl.—p. 218.
Histoplasmosis: Report of Case with Brief Review of Literature. B. Boltjes.—p. 226.

Michigan State Medical Society Journal, Lansing

42:497-576 (July) 1943

Prognosis After Injury or Infection of Nervous System in Childhood. B. Crothers.—p. 517.
Carcinoma of Larynx. D. F. Weaver.—p. 521.
Deafness or Impaired Hearing. G. E. Shambaugh Jr.—p. 525.
Diagnostic and Therapeutic Problems of Obesity. E. L. Sevringhaus. —p. 530.
Problem of Alcohol Addiction: Present Day Therapy. R. G. Tuck. —p. 536.
Radiocurability of Neoplasms. C. E. Nurnberger.—p. 541.
*Treatment of Psoriasis. L. A. Brunsting.—p. 546.

Treatment of Psoriasis.—The method recommended by Brunsting is the combined use of crude coal tar by inunction and of ultraviolet irradiation, a procedure first elaborated by Goeckerman. Crude coal tar ointment in a strength of from 2 to 6 per cent is used generally, excepting on the scalp and nails, where an ointment containing from 10 to 20 per cent ammoniated mercury is used. The patient is thoroughly bathed with soap and water to soften and facilitate removal of the scales. The trunk and extremities are thoroughly anointed with the tar ointment and suitable clothing is provided, such as loosely fitted underwear, pajamas or a covering of gauze. At bedtime additional ointment is applied to the body and scalp when needed. The next morning the tar ointment is smoothed with an oil to the consistency of a thin film over the entire body. Ultraviolet irradiation is carried out daily in increasing dosages. It is desirable to secure a brisk erythema short of a burn. Infiltrated plaques and the scalp may be subjected to more intensive treatment by protection of the surrounding skin by paper or cloth, but it is essential to irradiate the entire surface of the body. After the ultraviolet treatment a bath and shampoo again are in order and the ointments are reapplied. A considerable proportion of psoriatic persons also are subject to arthritis. The most common site of involvement in the early stages is the terminal phalanges of the fingers or toes; gradually the larger joints may become involved, even the spinal column, and when the disease is advanced the picture may resemble that of arthritis deformans. The treatment of psoriatic arthritis depends on prompt recognition and thorough control of the psoriasis by the use of crude coal tar and ultraviolet rays. The affected joints are treated as in other forms of arthritis. It is

wise to bring into play all the auxiliary forces, such as rearrangement of the diet and thorough elimination of foci of infection. Nonspecific treatment which provokes fever, such as hot baths, hyperthermy or the injection of foreign protein, is useful. Sun bathing is recommended strongly, and often a change to a sunny, dry and equable climate is beneficial. Roentgen therapy is practicable when there is early involvement of the joints of the hands and feet.

New England Journal of Medicine, Boston

228:773-808 (June 17) 1943

Medical Aspects of Absenteeism. L. R. Daniels.—p. 773.
Roentgenologic Diagnosis of Right-Sided Enlargement of the Heart. M. L. Sussman, A. Grishman and M. F. Steinberg.—p. 777.
Prognosis in Cases of Serofibrinous Pleurisy. J. E. Farber.—p. 784.
Epidemiologic Aspects of Food Borne Disease (continued). V. A. Getting.—p. 788.

228:809-840 (June 24) 1943

How Best to Eat Under War Conditions. F. J. Stare.—p. 809.
Spina Bifida and Cranium Bifidum: IV. An Unusual Nasopharyngeal Encephalocele. F. D. Ingraham and D. D. Matson.—p. 815.
Hemorrhage and Purpura Caused by Dicoumarin: Report of Case. A. Cahan.—p. 820.
Epidemiologic Aspects of Food Borne Disease (concluded). V. A. Getting.—p. 823.

229:1-32 (July 1) 1943

*Subdiaphragmatic Abscess in Children. W. E. Ladd and H. Swan.—p. 1.
Tidal Drainage and Cystometry in Treatment of Sepsis Associated with Spinal Cord Injuries: Study of 165 Cases. D. Munro.—p. 6.
Hip-Nail Determiner. A. R. Gardner and G. Middlebrook.—p. 14.
Peripheral Vascular Disease. R. W. Wilkins and C. K. Friedland.—p. 16.

Subdiaphragmatic Abscess in Children.—A subdiaphragmatic abscess complicating the postoperative course in a 3 year old boy with a ruptured appendix induced Ladd and Swan to review the cases previously seen at the Children's Hospital of Harvard Medical School. Fourteen patients have been seen in whom an abscess in the subdiaphragmatic space has been recognized. Eleven of these were treated surgically with one death; the other 3 had a fulminating infection and died. Post mortem a subphrenic abscess was found as one among multiple manifestations of a generalized sepsis. The symptomatology of subdiaphragmatic abscess showed considerable variation in the reviewed cases, but it appears that in children at least three different types are encountered. These roughly parallel the different modes of origin of the infection. The first group comprises cases in which the subphrenic infection is part of a widespread intra-abdominal suppurative process. The second group, in which the subphrenic infection complicates the course of an acute appendicitis with rupture of the appendix, is the type most commonly seen. The third group, perhaps the most interesting and difficult to diagnose, comprises cases in which the subphrenic abscess is metastatic and is at once the chief or only disease present. These patients have a history of upper respiratory infection, otitis media or recurrent superficial staphylococcic infection. This is followed some days later by the vague and insidious onset of mild malaise and anorexia associated with low grade pyrexia. These symptoms persist and there begin occasional attacks of abdominal pain. These symptoms gradually increase over a period of one to three months until the patient is brought to the hospital because of the appearance of a mass in the upper part of the abdomen. It is generally agreed that early and adequate drainage is the correct treatment for subphrenic abscess. In this series 11 patients underwent operation for drainage of a subphrenic abscess, with one death, a mortality of 9 per cent. There were 5 cases in which a direct incision was made and 2 in which the peritoneum was stripped from the diaphragm, making 7 in which there was an extraserous approach. These patients had a much shorter and better convalescence than did those who had a trans-serous approach. The extraserous approach is the one of choice.

New Orleans Medical and Surgical Journal

95:531-578 (June) 1943

Hypogastric Sympathectomy with Special Reference to Surgical Anatomy of Superior Hypogastric Plexus. B. B. Weinstein.—p. 534.
Human Serum and Plasma in Diseases of Children. E. S. Platou.—p. 547.
Duodenal Diverticulitis, Acute and Chronic. D. C. Browne and G. McHardy.—p. 553.
Bagasse Disease of Lung. W. A. Sodeman and R. L. Pullen.—p. 558.

New York State Journal of Medicine, New York

43:1183-1278 (July 1) 1943

Summary of Present Treatment of Wounds and Burns. R. Hayden.—p. 1213.
Recent Trends in Psychotherapy. L. R. Wolberg.—p. 1220.

43:1279-1374 (July 15) 1943

Treatment of Severely Burned Patient with Special Reference to Controlled Protein Therapy. E. B. Mahoney and J. W. Howland.—p. 1307.
Urology in Industry. G. E. Slotkin.—p. 1316.
Urinary Extravasation (Periurethral Phlegmon): New Concept of Pathogenesis and Treatment. E. O. Finestone.—p. 1320.
Epididymitis: Its Relationship to Trauma and Compensation. R. B. Henline and W. Yunck.—p. 1325.
Study of Headaches Following Diagnostic Spinal Taps. H. Adler.—p. 1328.
Vitamins for Gray Hair. J. J. Eller and L. A. Diaz.—p. 1331.
Lesions of Anorectal Region Associated with Symptoms of Prostatism. J. A. Lazarus.—p. 1333.
Thyroidectomized Patients After Ten Years: Analysis of 100 Consecutive Cases. A. H. Noehren.—p. 1338.

North Carolina Medical Journal, Winston-Salem

4:197-240 (June) 1943

President's Address: Immediate Responsibility of Organized Medicine. D. B. Cobb.—p. 197.
Psychotherapy Within Psychosomatic Medicine. M. H. Greenhill.—p. 203.
Hormonal Approach to Carcinoma of Prostate. E. P. Alyea and A. F. Henderson.—p. 212.
Roentgen Manifestations of Gout. S. Kamberg.—p. 219.

4:241-272 (July) 1943

Functions of County Medical Society. G. L. Carrington.—p. 241.
Requisites of Good County Medical Society President. V. S. Caviness.—p. 242.
Functions of County Medical Society Secretary. O. L. McFadyen.—p. 245.
Treatment of Hypertension in Light of Modern Experimental Investigations. A. Grollman.—p. 246.
Some Aspects of Mental Hygiene or Preventive Psychiatry. J. W. Vernon.—p. 251.
Acute Leukemia as Terminal Event in Polycythemia Vera: Report of 2 Cases with Autopsies. O. C. Hansen-Pruss and E. G. Goodman.—p. 254.
Foreign Body in Stomach: Report of Unusual Case. H. M. Starling and C. R. Duncan.—p. 258.

Public Health Reports, Washington, D. C.

58:857-892 (June 4) 1943

Caries: Fluorine Hypothesis and Suggested Study to Test Its Application. D. B. Ast.—p. 857.

58:893-936 (June 11) 1943

Blueprint for Conquest of Hunger. T. Parran.—p. 893.
*Dermatitis from Resin Glue in War Industries. L. Schwartz, S. M. Peck and J. E. Dunn.—p. 899.
Activities of State and Local Industrial Hygiene Services in War Year. Victoria M. Trasko.—p. 904.

58:937-968 (June 18) 1943

Poliomyelitis in United States in 1942 and Summary of Its Prevalence from 1933 to 1942 Inclusive. C. C. Dauer.—p. 937.
Leptospirosis in Rats (R. Norvegicus) In and About Washington, D. C.: Evaluation of Methods Used for Diagnosis. C. L. Larson.—p. 949.
Effect of Arsenates on Storage of Lead. L. T. Fairhall, J. W. Miller and F. L. Weaver.—p. 955.

Dermatitis from Resin Glue in War Industries.—Schwartz and his associates point out that an increase in the use of glues in the manufacture of wood substitutes has resulted in an increase in occupational dermatitis among workers in these industries. Glues can be classified with respect to their composition as (1) protein glues, (2) natural resin glues, (3) synthetic resin glues and (4) combinations of the foregoing. In the factories inspected in the course of this study the urea-formaldehyde and the phenol-formaldehyde resin adhesives caused most of the dermatitis. In making plywood for planes and gliders, those who apply the cold liquid glues and those who apply the glue tapes are the ones most likely to be affected with dermatitis. The parts most often affected are the palms. The dermatitis begins in some workers as early as the third day after exposure (the primary irritant effect of the glue), while other workers may be exposed several weeks before it occurs. In factories where glass cloth is used workers thought the glass fabric was the cause of the dermatitis but patch tests

showed that the phenol-formaldehyde molding powder was responsible. The treatment for dermatitis caused by glues is the same as for other forms of contact dermatitis. Where there are edema, vesicles and oozing, only soothing wet dressings should be used, such as solution of boric acid, solution of aluminum acetate (Burow's solution) and 3 to 5 per cent tannic acid solution, this last on parts other than the face or neck. When the eruption begins to dry and crust, mild fatty base ointments such as those of boric acid, calamine or zinc oxide should be used. Workers with mild eruptions should be given protective clothing and should be treated on the job in order to give them the chance to become "hardened" (if the dermatitis is caused by allergy) and to learn how to protect themselves (if it is due to primary irritation). To prevent dermatitis the management should provide suitable exhausts to draw away all irritant dusts or fumes. Clean coveralls should be provided daily for workers exposed to irritant glues, dusts and fumes. Workers who apply the glues should be provided with impervious gloves made either of washable leather or fabric lined rubber and sleeves and aprons of impervious materials. The sleeves should fasten over the gloves at the wrist to prevent irritants from falling into the gloves. Facilities should be provided so that workers can frequently wash glue from the gloves and the skin. The brushes and the sponges used for gluing should be washed or changed about every two hours, and workers should be cautioned against touching the face and other parts of the body with glue soiled fingers, gloves or tools.

Surgery, St. Louis

14:1-156 (July) 1943

Crile, Kelly, Lane. R. Matas.—p. 1.
Kenny versus Orthodox Treatment of Anterior Poliomyelitis. J. A. Key.—p. 20.
Acute Perforated Gastric and Duodenal Ulcers. F. X. Paletta and W. R. Hill—p. 32.
Actinomycosis of Stomach and Duodenum: Report of 2 Cases. E. W. Shearburn.—p. 38.
Lipomas of Gastrointestinal Tract with Special Reference to Small Intestine Including Ileum: Review of Literature and Report of 6 Cases. L. E. Schottenfeld.—p. 47.
Rectal Stricture Due to Lymphogranuloma Venereum: Treatment with Sulfonamide and Frei Antigen. H. R. Seidenstein.—p. 73.
Murphy Button in Esophagogastrostomy. L. Miscall and B. B. Clark. —p. 83.
*Renal Circulation After Compression of Renal Artery According to Method of Goldblatt: Study of Influence of Renal Venous Runoff on Experimental Hypertension. F. P. Corrigan and I. Pines.—p. 88.
*Sulfonamide Therapy in Actinomycotic Infections. C. Lyons, Cora R. Owen and W. B. Ayers.—p. 99.
Solitary Eosinophilic Granuloma: Report of Case. G. A. Kernwein and F. B. Queen.—p. 105.
Study of Physical Factors Concerned in Inflammation: III. Fixation of Bacteria in Inflamed Tissues. C. J. Bellis.—p. 111.
Unusual Intra-Abdominal Foreign Body. H. T. Wikle.—p. 122.
Traumatic Rupture of Spleen with Delayed Hemorrhage: with Reference to Condition as Complication of Rib Fractures; Report of 2 Cases. R. L. Waugh and J. A. Prior.—p. 125.
Surgical Significance of Middle Palmar Septum of Hand. J. E. Flynn.—p. 134.
Early Postoperative Walking: II. Collective Review. B. Newburger. —p. 142.

Renal Circulation After Compression of Renal Artery.—The purpose of this study by Corrigan and Pines was to check whether and to what degree the ischemia of renal tissue shares in the production of hypertension and, if not, which other factor can be made responsible for the appearance of high blood pressure. They examined the possibility of arterial hypertension being dependent on the relative increase of local venous pressure as compared to the pressure on the arterial side of the kidney. They sought to increase the venous runoff and to diminish the venous pressure after the Goldblatt maneuver had been performed. In order to accomplish this they elevated the kidneys sufficiently to straighten the course of the renal veins. This added the force of gravity to the vis a tergo in certain positions of the animal, prevented the collapse of venous walls and, by establishing a closer contact between the renal vein and artery, increased the effect of arterial pulsation on the movement of blood in the renal vein. This procedure was applied only to animals that had developed hypertension. In the first group of dogs the procedure was applied to kidneys the renal arteries of which were previously constricted, in the second group of dogs to the intact opposite kidney with simultaneous ligation of the renal artery so that both renal arteries were ligated and only one kidney was elevated, and in the third group of dogs to the intact opposite kidney without ligating the ipsilateral artery, so that one renal artery was ligated and the opposite kidney elevated in the manner already described. In all cases there was a decided fall of blood pressure. These results were particularly striking in the second group, in which, following constriction of both arteries, a further increase of blood pressure could be expected. Results of their experiments are confirmed by the clinical experience of McCann and Romansky and of Riskind and Greene, who have established that the hypertension which accompanies the renal ptosis or renal torsion can be actively eliminated as soon as the incorrect position of the kidney is improved by a surgical operation or by an abdominal belt. The decisive factor, however, in the authors' opinion consists not in the reduction of the lumen of the renal artery because of the renal ptosis but in the impeding of the venous outflow in these conditions and in the fact that the restoration of the kidneys to their right place has had its effect on arterial blood pressure through improvement of the venous return. They conclude that hypertension depends on the disturbance of the balance between the pressure on the arterial and on the venous side of the kidney. When this balance is disturbed in favor of the venous pressure, stasis probably takes place in the renal capillaries and primary renal circulation is short-circuited through arteriovenous shunts. Consequently the tissue responsible for hypertension begins to suffer from inadequate supply of blood and production of a hypertensive substance is begun. When the balance between the pressure in the arterial and venous sides of the kidney is restored the production of hypertensive substance will cease, perhaps through reestablishment of an efficient oxygenation.

Sulfonamide Therapy in Actinomycotic Infections.—The 5 cases of actinomycotic infections reported by Lyons et al. emphasize the necessity for long and continuous sulfonamide administration to effect healing and maintain remission of the disease. Sulfanilamide supplemented the surgical management of 5 patients infected with actinomyces. The etiologic agent was an anaerobic Actinomyces bovis in 4 cases: one cervicofacial, one pulmonary, one pulmonary and abdominal and one abdominal infection. An aerobic non-acid fast actinomyces was found in another case in which there was an abscess of the buttocks. In every instance clinical improvement was noted within the first three weeks of sulfonamide treatment. This improvement was not maintained unless the sulfonamide compound was continued for a considerably longer period of time. Nine months of treatment with 4 Gm. daily produced healing for two years in 1 case. Other patients treated with smaller doses for equal or longer periods of time showed recurrent abscesses and fistulous sinuses, but all patients appear improved. The dramatic initial response of these infections to sulfonamides is somewhat misleading. The drugs induce a remission and apparently diminish the intensity of the recurrence, but it can hardly be claimed that the disease has been completely cured. The necessity of surgical excision of the infection is clear. Surgical excision of all the infected tissue is the most effective treatment of the disease. Sulfonamide therapy is a valuable adjuvant to the surgical management of actinomycotic infections.

West Virginia Medical Journal, Charleston

39:233-264 (July) 1943

Optic Atrophy. F. V. Gammage.—p. 233.
Pharyngoesophageal Diverticulum Treatment by One Stage Disposition of Sac. R. H. Edwards.—p. 241.
Use of Serum, Plasma and Blood in Gynecology and Obstetrics. A. P. Hudgins.—p. 243.
Virus Pneumonia. W. C. Stewart.—p. 248.
Catalase and Peroxidase in Pathologic Urine. L. I. Halley.—p. 252.

Wisconsin Medical Journal, Madison

42:657-748 (July) 1943

Prostatic Surgery at Wisconsin General Hospital, 1940-1941. I. R. Sisk and P. M. Cornwell.—p. 679.
Cesarean Section Problem in Wisconsin. R. S. Cron.—p. 683.
Clinical Applications and Complications of Sulfonamides. W. W. Spink.—p. 688.
Modern Status of Sulfamido Group of Drugs Used in Urology. T. L. Pool.—p. 693.
Roentgen Study of Virus Pneumonia. H. P. Doub.—p. 696.
Present Day Treatment of Varicose Veins. H. O. McPheeters. —p. 701.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Journal Obst. & Gynaec. of Brit. Empire, Manchester

50:161-240 (June) 1943

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Further Investigations on Histidine and Histamine Metabolism in Normal and Pathologic Pregnancy. R. Kapeller-Adler.—p. 177.
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Primary Abdominal and Primary Ovarian Pregnancy, with Report of 1 Case of Each Variety. R. C. Thomas.—p. 189.
Puerperal Tetanus, with Report of Case Following Septic Criminal Abortion. R. C. Thomas.—p. 196.
Prognostic Significance of Rise in Temperature in Course of Radium Treatment of Cancer of Cervix. Gertrude Goldscheider.—p. 202.
Unusual Case of Intraperitoneal Bleeding from Ruptured Uterine Vein During Pregnancy. Kathleen M. D. Harding and A. B. Concanon.—p. 208.
Excretion of Ketosteroids in Human Pregnancy Urine in Relation to Sex of Fetus. H. Burrows, D. MacLeod and F. L. Warren.—p. 212.
Division of Zygote Producing Trophoblast Only. V. Bonney.—p. 217.
Intrapelvic Tuberculosis. J. R. Goodall.—p. 219.
Local Anesthesia in Vulval and Vaginal Surgery. C. P. Brentnall.—p. 226.

Lancet, London

2:33-62 (July 10) 1943

Sensory Areas of Brain. E. D. Adrian.—p. 33.
Pulmonary Tubercle in Children: Influence of Evacuation on Its Incidence. Marcia Hall.—p. 35.
*Bactericidal Action of Estrogens. G. H. Faulkner.—p. 38.
Gunshot Aneurysm of Carotid Artery. R. S. Handley and M. Oldfield.—p. 40.
Pellagra in Psychiatric Practice: Twelve Recent Cases. S. W. Hardwick.—p. 43.

Bactericidal Action of Estrogens.—Faulkner observed that diethylstilbestrol possesses some degree of bactericidal activity. Other substances possessing estrogenic properties were examined in order to see whether there was any correlation between the estrogenic and the bactericidal activities. Estradiol, estrone, diethylstilbestrol, hexestrol and diethoxytriphenylbromoethylene were investigated. The organisms used were all recently isolated from material sent to the laboratory for bacteriologic investigation. The strains of Corynebacterium diphtheriae were all virulent to guinea pigs. All the hemolytic streptococci exhibited beta hemolysis, and strains 4, 5 and 6 belonged to Lancefield's serologic group A. Faulkner states that diethylstilbestrol is bactericidal and in lesser concentrations bacteriostatic to gram positive cocci, Corynebacterium diphtheriae and Neisseria catarrhalis. No inhibitory action was noted on the gram negative bacilli. The minimal lethal concentration varies somewhat between these organisms, but in all those recorded it lies between 1 : 5,000 and 1 : 500,000. Tubercle bacilli were killed by incubation in vitro with diethylstilbestrol 1 : 5,000. Hexestrol also possesses bactericidal properties. Other estrogenic substances (estrone, estradiol and diethoxytriphenylbromoethylene) have not been found to have bactericidal action. The bactericidal activity of diethylstilbestrol is reduced in the presence of serum.

2:63-90 (July 17) 1943

Anaerobic Infections of War Wounds in Middle East. J. D. MacLennan.—p. 63.
March Fracture: Series of 15 Cases from R. A. F. G. Flavell.—p. 66.
*Bacillary Dysentery: Chemotherapy in Its Treatment; An Experience of 492 Cases in Middle East. E. Bulmer and W. M. Priest.—p. 69.
*Sonne Dysentery: Sulfapyridine in Its Treatment. R. Swyer.—p. 71.
*Propamidine in Surgical Infections: Clinical Study. E. C. B. Butler.—p. 73.
Method of Producing Experimental Granulating Wounds. H. E. Hutchison.—p. 75.

Bacillary Dysentery.—Bulmer and Priest assess the value of chemotherapy in bacillary dysentery on the basis of experience of eighteen months in the Middle East covering two summers. A sorting of cases by stool inspection shows two groups; there is the mildest type without blood and mucus in the stools familiarly known as "Gyppy tummy" and arbitrarily called acute catarrhal enteritis; this is an unpleasant condition, often febrile, associated with considerable abdominal pain and frequently needing hospital treatment. Even in this "mildest" type the stay in hospital of 600 patients averaged ten days. True dysentery is distinguished by the presence of blood and mucus in the stools and is a much graver disease; the average duration of stay in the hospital of 600 patients was twenty days. A series of 483 patients with nonamebic diarrheas, the majority being bacillary dysentery, were treated with sulfonamide drugs. Of 323 patients treated with sulfaguanidine the average stay in the hospital was substantially reduced as compared with that of 600 controls. Of 97 patients with acute dysentery treated with sulfapyridine the stay also was reduced, but the patients experienced nausea, vomiting and malaise. Of 63 patients treated with sulfanilamide the stay in the hospital was not reduced. The authors conclude that: 1. Sulfaguanidine is a specific drug in the treatment of acute, subacute and chronic bacillary dysentery; it is almost nontoxic and does not upset the patient. It is probable that its routine use would diminish the stay in the hospital by one half. 2. Sulfanilamide in the form of crushed tablets does not have any definite effect in dysentery. 3. Sulfapyridine is of considerable value in dysentery but is not so effective as sulfaguanidine. Its unpleasant effects make its use undesirable unless sulfaguanidine is not available.

Sulfapyridine in Sonne Dysentery.—According to Swyer the incidence of Sonne dysentery has been increasing in Britain. Consequently any procedure which shortens the illness or reduces the number of carriers becomes of great importance. The series here described comprised 92 patients with Sonne dysentery, 57 of whom were treated with sulfapyridine and 35 were used as controls. Except at week ends, daily bacteriologic examinations of feces and rectal swabs were done in all chemotherapy series, and twice weekly in controls, on desoxycholate-citrate agar. Treatment with sulfapyridine by mouth was instituted immediately on isolation of Bacterium sonnei and was continued until a negative report on the feces and on rectal swabbing was obtained. Administration of the drug was then stopped and after an interval of forty-eight hours further bacteriologic examinations were made. If these proved negative, examinations were repeated until a minimum of three consecutive negative stools and rectal swabs had been obtained. If after forty-eight hours the stool or rectal swabbing reverted to positive, the course of treatment was repeated. Careful watch was kept for toxic symptoms of chemotherapy, granulocytopenia being guarded against by leukocyte counts. In the chemotherapy group the average time required to obtain bacteriologic clearance was a fourth of that in the control group (five compared with twenty-one days). The period required to obtain apparently normal stools in the chemotherapy group was halved (nine compared with twenty days). No bacteriologic relapses after three days of the negative state arose in the drug treated patients but in controls six such relapses developed at periods ranging from seven to thirty-six days after apparent clearance.

Propamidine in Surgical Infections.—Butler points out that propamidine has been shown to retain its bacteriostatic action in the presence of pus in concentrations which do not prevent phagocytosis, a property which makes it useful in the treatment of infected wounds. The drug is effective in staphylococcic infections and is extremely potent against the hemolytic streptococcus but is of little use against Proteus vulgaris and Pseudomonas aeruginosa; in vitro against Clostridium welchi the activity is probably of the same order as against Staphylococcus aureus. The present paper describes a series of cases and suggests an additional method of using the drug. Two preparations have been employed, a jelly or a solution. Of 10 cases reported, 7 illustrate the value of propamidine jelly in the treatment of recent war wounds, infected hands and certain types of bone infection; 3 show that a 1 per cent solution of propamidine injected into infected joint or empyema cavities may help to overcome the infection and sometimes make surgical intervention unnecessary. The jelly base of the propamidine preparation is a tissue irritant and must not be used if the wound is to be sutured. When used round open wounds it may cause redness of the skin, which should be protected by petrolatum. If the drug is used for more than ten days the production of granulation tissue is often stimulated to an extent which is undesirable in superficial lesions but useful in filling up deep cavities. Propamidine jelly does not penetrate soft tissues or bone and is essentially a local bacteriostatic. Propamidine solution has mainly been used against staphylococcic infections.

Medicina, Buenos Aires

3:259-385 (April) 1943. **Partial Index**

Importance of Bile in Absorption of Vitamin K. R. Bay, C. A. Tanturi and R. F. Banfi.—p. 259.
*Compensatory Myeloid Metaplasia of Spleen: Importance of Differentiation from Chronic Myeloid Leukemia. A. Pavlovsky.—p. 287.
Sudden Death. A. C. Taquini and L. de Soldati.—p. 328.

Compensatory Myeloid Metaplasia of Spleen.—Pavlovsky stresses the importance of a differential diagnosis between compensatory myeloid metaplasia of the spleen in aplasia of the myelopoietic organs and chronic myeloid leukemia. He observed 7 cases of the former condition and 99 cases of the latter. High voltage roentgen irradiation of the spleen, indicated in chronic myeloid leukemia, is contraindicated in compensatory myeloid metaplasia. A diagnosis of compensatory myeloid metaplasia of the spleen is made on clinical symptoms similar to those of chronic myeloid leukemia but of long duration, acute splenomegaly, changes in the peripheral blood similar to those of chronic myeloid leukemia or of chronic myeloid subleukemia, certain changes of the long bones and lack of tenderness over the sternum. The diagnosis should be verified by the examination of the sternal bone marrow and of spleen tissue obtained by puncture. The bone marrow is either aplasic or hypoplasic, whereas the splenic tissue is transformed into myeloid tissue. In 5 of the group of 7 cases of compensatory myeloid metaplasia of the spleen reported by the author, roentgen irradiations of the spleen were done. The 3 patients who received large doses of roentgen rays to the spleen rapidly developed symptoms of acute panmyelophthisis, aplastic anemia and thrombopenic purpura respectively. Immediate discontinuation of irradiation and attempts to control the disease failed. Two patients who had weekly irradiations with small doses rapidly grew worse. The symptoms were controlled by immediate discontinuation of the irradiations and the exhibition of hematonics. The last 2 patients and those given hematonics are living and are in a fairly good state of health. One of them is still living with compensatory myeloid metaplasia of more than twenty years' duration.

Medicina, Mexico, D. F.

23:205-230 (June 25) 1943. **Partial Index**

Pathology of Brucellosis. H. Tavar Mancera.—p. 205.
*Natural Infection of Cats with Typhus. L. Mazzotti and G. Varela.—p. 229.

Natural Infection of Cats with Typhus.—Mazzotti and Varela experimented on domestic cats living in or near the wing for patients with infectious diseases in the General Hospital of Mexico City. Agglutination tests for Proteus typhi gave positive results with the blood of the animals. The tests were strongly positive with the blood of some animals. Guinea pigs inoculated with the brain of either cadavers of patients who died with typhus or of rats that had been previously inoculated with the brain of the cats developed fever and scrotal inflammation (Neill-Mooser positive sign). Extracellular and intracellular rickettsiae in large numbers were observed in cultures of the tunica vaginalis of inoculated guinea pigs. The authors direct attention to the presence of natural typhus in domestic cats and the possible role of these animals as temporary reservoirs of typhus. Natural infection of cats probably occurs through fleas or through ingestion of infected material.

Prensa Médica Argentina, Buenos Aires

30:689-734 (April 21) 1943. **Partial Index**

Hyperinsulinism Due to Adenoma of Insular Cells: A. Ceballos and S. Rosenblatt.—p. 689.
*Procaine Hydrochloride Spinal Anesthesia and Altitude: P. Perovic.—p. 706.
Traumatic Hernia of Testicle. D. Calisti.—p. 709.

Spinal Anesthesia and Altitude.—Perovic found that the effects of spinal anesthesia induced with procaine hydrochloride diminished with increase in altitude. The dose varies in the following proportions: from 0.08 to 0.10 Gm. at altitudes of 500 meters over sea level, from 0.10 to 0.12 Gm. at altitudes between 1,000 and 1,500 meters, from 0.12 to 0.14 Gm. at altitudes between 2,000 and 2,500 meters, from 0.14 to 0.16 Gm. at altitudes between 3,000 and 4,000 meters and from 0.14 to 0.17 Gm. at altitudes over 4,500 meters above sea level. The author believes that increased altitude causes increased concentration of organic and chemical substances in the cerebrospinal fluid, which is the factor in diminishing the effect of the anesthetic on the central nervous tissues.

Revista de la Asoc. méd. Argentina, Buenos Aires

57:149-218 (April 15-30) 1943. **Partial Index**

*Pulmonary Blastomycosis with Cavitation. E. L. Capdehourat, R. A. Gini and M. E. Jörg.—p. 149.
Sulfanilamide in Surgery. J. Nasio.—p. 157.
Antidiuretic Action of Pitressin in Acute Nephritis. R. Q. Pasqualini and A. C. Avogadro.—p. 168.
Therapy of Obstetric Shock. G. Ricci, N. Rodriguez Miranda and M. Balaguer.—p. 175.

Pulmonary Blastomycosis with Cavitation.—According to Capdehourat and his collaborators pulmonary blastomycosis with cavitation is rare. The case they report is the second in the literature. A woman aged 26 presented symptoms simulating pulmonary tuberculosis of five years' duration. The bacteriologic examination of the sputum was negative for tubercle bacilli but showed numerous monilia. X-ray examination of the lung showed a shadow of a large solitary cavity. Sulfonamide therapy was without effect. Intravenous injections of chiniofon in doses of from 5 to 10 cc. and sodium iodide or potassium iodide in daily dose of 0.4 Gm. brought about a clinical and roentgenologic cure of the patient. Repeated x-ray examinations of the lung demonstrated disappearance of the cavity more than eight months after discontinuation of the therapy.

Zentralblatt für Chirurgie, Leipzig

69:81-128 (Jan. 17) 1942. **Partial Index**

Radium Treatment of Hemangiomas in Children. E. Günsel.—p. 82.
*Malignant Exophthalmos. P. Sunder-Plassmann.—p. 88.
*Fatigue Fractures and Zones of Transformation in Bone. F. Schröder.—p. 92.

Malignant Exophthalmos.—According to Sunder-Plassmann there are cases of exophthalmic goiter in which the exophthalmos continues to increase after removal of the thyroid. These are cases of malignant exophthalmos. In the mild form of malignant exophthalmos conjunctival excision has been effective, but there are also cases in which the exophthalmos increases to a point of perforation of the eye. The author reports a case in which enucleation of the eyes became necessary. In another case conservative measures proved ineffective. Both eyes had advanced corneal ulcers, and spontaneous perforation seemed imminent. The patient required morphine for the control of the pain. The visual capacity was practically nil. As a last resort it was decided to attempt the operation described by Naffziger in 1933, which that author had successfully employed in 6 cases. Bilateral trepanation was done and then by the intracranial approach complete orbital decompression was effected, also decompression of the roof of the nerve canal. As had been observed by Naffziger, the eye muscles were enormously enlarged and both optic nerves showed extreme edema. The patient tolerated the operation well. The exophthalmos receded rapidly, and complete closure of the eyes became again possible. The corneal ulcers healed. The patient regained normal visual capacity and her general condition is excellent.

Fatigue Fractures.—Schröder shows that the pathologic changes caused by overexertion of bones become manifest in two distinct forms: as fatigue fracture and as "umbauzone" (zone of transformation). The fatigue fracture represents a typical fracture. The fracture line is usually delicate, there is considerable callus formation and the pain is severe. The zone of transformation shows a wide area of reduced density, but there is only slight or no callus formation and mild pain. Both lesions are observed at the characteristic sites of greatest exertion, but, whereas fatigue fracture occurs only in healthy bone tissue, zones of transformation develop chiefly in the presence of metabolic disturbances or deficiency diseases. The author reports that zones of transformation appeared in both scapulas, both rami of the os pubis and on the eighth rib on the left side of a woman aged 42. These zones of transformation disappeared after prolonged treatment with vitamin C, and it is concluded that vitamin deficiency played a part in their development.

Book Notices

Health and Physical Fitness. By I. H. Goldberger, M.D., Assistant Director of Health Education, New York City Public Schools, and Grace T. Hallock, Director, Welfare Publication Bureau, Metropolitan Life Insurance Company. Cloth. Price, $1.92. Pp. 596, with illustrations. Boston: Ginn and Company, 1943.

This book by two authors experienced in health education is designed specifically to contribute to the training in health and physical fitness of the high school Victory Corps and in general for high school health education programs. It follows a conventional organization of such textbooks but is exceptionally rich in well conceived illustrations used in the modern manner, including bleedoff, montage, diagrammatic section and partial section technics. Each unit has a challenging set of questions under the title "What Would You Think, Say, or Do If—" and under each of these titles such challenging questions as "A 4 year old child of your acquaintance lost a tooth and his mother said 'It doesn't matter; he'll get another to take its place'?" There are also matching tests, true-false selections, completion tests, extensive suggestions for further study and discussion, and a list of scientific words of which to learn the meaning. Each unit is introduced by a set of "leading questions." The units are effectively entitled; for example, the unit on vision is called "Look!" and, in the same manner, that on hearing "Listen!" The book is interestingly presented and thoroughly practical. It should be a valuable teaching help.

The Pharmacology of the Opium Alkaloids. Part 2. By Hugo Krueger, Assistant Professor of Pharmacology, St. Louis University School of Medicine, Nathan B. Eddy, Principal Pharmacologist, U. S. Public Health Service, and Margaret Sumwalt, Associate Physiologist, U. S. Public Health Service. Supplement No. 165 to the Public Health Reports. Federal Security Agency, United States Public Health Service, Division of Sanitary Reports and Statistics. Cloth. Price, $1.50. Pp. 813-1448. Washington, D. C.: Supt. of Doc., Government Printing Office, 1943.

The first part of this book offered a dissertation on morphine which provided an excellent informative source for reference. The second part is intended to supplement the other volume and offers concise presentation of pertinent data on codeine, ethylmorphine, dihydromorphinone, diacetylmorphine, thebaine, apomorphine, other derivatives of morphine, sinomenine and its derivatives, papaverine and its derivatives, narcotine and its derivatives, narceine and its derivatives, cryptopine and protopine. The book is not for the practicing physician unless he has an unusual interest in the opium alkaloids; it should be available for all teachers and researchists in pharmacology and therapeutics. The material is presented in concise form and its accumulation must represent the labor of almost uncountable searches into the literature by the authors. The bibliography, subject and author indexes are as complete as the reviewer has ever seen.

Urology in General Practice. By Nelse F. Ockerblad, B.S., M.D., F.A.C.S., Professor of Clinical Urology, University of Kansas School of Medicine, Lawrence, and Hjalmar E. Carlson, B.S., A.M., M.D., Instructor in Urology, University of Kansas School of Medicine. Cloth. Price, $4. Pp. 383, with 98 illustrations. Chicago: Year Book Publishers, Inc., 1943.

Had the authors of this little volume adhered to their promise as stated in the preface "to help the general physician do better those things that are within his province in the realm of genitourinary diseases and to suggest the limits beyond which the best interests of his patients require that he obtain the help of a specialist," this might have been a book of value, but unfortunately they fall far short of the mark. The text starts with the most elementary details of laboratory diagnosis and presently one finds an adjoining chapter on such subjects as kidney ptosis, anomalies of the genitourinary tract and urinary lithiasis, the subject matter of which might cause even a research worker to ponder. The reviewer takes issue with the discussion of nephritis. This chapter may be comprehensive but it has no place in urology. Nephritis is a medical disease. There is no sequence whatever to the arrangement of the subject matter, no orderly presentation, even though isolated topics are well discussed. It is most unfortunate that an experienced urologist should write about diseases of the male urethra to the complete exclusion of pathology of the verumontanum, about which the general practitioner should know, even though he is not equipped to treat it, and so on. In brief, this book is neither fish nor fowl; it is smörgåsbord.

Index to Dental Literature in the English Language Including One Hundred and Twelve Periodicals from Australia, Canada, England, India, South Africa and the United States. Three Years, 1939-1941. An Alphabetical Subject and Author Index, A List of Dental Books. Committee on Library and Indexing Service of the American Dental Association. John E. Gurley, D.D.S., Chairman. Cloth. Price, $7.50. Pp. 282. Chicago: American Dental Association, 1943.

The American Dental Association is to be congratulated on the appearance of this volume of the "Dental Index," covering the years 1939 to 1941, in which a change of style has been effected. Instead of the former numerical system of classification the arrangement is alphabetical according to author and subject. Listing of entries under subjects by title rather than by author and the use of continued column heads would have improved the make-up still further. The subject headings are practical rather than scholarly, but they represent nomenclature in current use. It is hoped that certain wordy headings, inconsistencies in indexing and similar technical defects will be eliminated in future volumes.

How to Prepare for Military Fitness. By Lieutenant Colonel François D'Eliscu. Illustrated by Stephen J. Voorhies. Cloth. Price, $1.96. Pp. 216. New York: W. W. Norton & Company, Inc., 1943.

In this compact volume there is an excellent, well edited and adequately illustrated description of the more important methods of physical training. The material is carefully selected from among the more beneficial forms of calisthenics and conditioning exercises as they apply to military personnel. Descriptions of drills, exercises and games are concisely vivid and accurate. The author has subtly drawn on his own experience to add to the effectiveness of the instructions given. Wall scaling and tree climbing, elementary judo, wartime wrestling and boxing, unarmed defense and disarming an opponent are especially valuable and timely chapters. Further, to meet current needs, the last portion of the book adequately describes swimming and life saving procedures to be employed in common situations which soldiers and sailors are apt to encounter. Throughout there are many well drawn black and white illustrations which clarify the subject. On the whole it is an excellent handbook on physical training that deserves a wide circulation.

Your Own Story. By Marion L. Faegre, Assistant Professor of Parent Education, Institute of Child Welfare, University of Minnesota, Minneapolis. Paper. Pp. 52, with illustrations. Minneapolis: Minnesota Department of Health, 1943.

This booklet contains a brief story of human and animal reproduction—not animal and human—to which thirty-one of its fifty-two pages are devoted. The remainder is a chapter addressed to parents as to how to use the material in the first part of the pamphlet. The pamphlet could not be more effectively reviewed than in the words of Dr. Haven Emerson contained in its introduction: "Other states and, in fact, our federal agencies promoting human welfare could not do better than follow Minnesota's example and compete in friendly rivalry of word and design to carry to all parents and children lessons of the hygiene of human reproduction and the bearing of our bisexual structures and functions on personal, family and social soundness of character and happiness. What is here offered is to be unreservedly accepted and recommended for its accuracy and directness of statement and for the spirit and purpose of the language and illustrations used."

Memoirs of a Guinea Pig or Eight Years in a Doctor's Waiting Room. By Howard Vincent O'Brien. Cloth. Price, $2. Pp. 238, with illustrations by Robert Mills. New York: G. P. Putnam's Sons, 1942.

In his middle 40's Mr. Howard Vincent O'Brien, who is a clever writer, developed difficulty with his vision—a condition commonly referred to as scotoma. In his search for relief he tried everything, including shock therapy, heat therapy, allergy, manipulation of the feet, vitamins, osteopathy, chiropractic and procedures directed toward the intestines and the gallbladder. Apparently he comes to the end of 237 pages still with the scotoma, also with the ability to write an intensely human chapter on "The Care and Feeding of Doctors." Here he disports himself by injecting a few barbs into some of the easily recognized and significant weaknesses of the profession. In the course of his travels he came also under the attention of some of our leading ophthalmologists, who will be recognized not only by the mention of their names in the dedication but also by their characterization in the work. This item is recommended especially to ophthalmologists with a sense of humor but also to every doctor with a sense of humor.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

RUPTURE OF MEMBRANES TO INDUCE LABOR

To the Editor:—For over five years my colleagues and I have been inducing labor by artificial rupture of the membranes when we felt that this was indicated, that is, mainly when the child is past due with the head engaged or there is a plus 1 or plus 2. After the reorganization of our hospital staff we were told that this is poor obstetrics and will no longer be tolerated. We have never had a complication, which is probably due to the fact that we have never used this method promiscuously. We are interested mainly in determining whether or not this is generally considered a poor obstetric procedure. We should appreciate an opinion that will help answer this problem. If this procedure is poor obstetrics we wish to discontinue it; however, the fact that we have used it successfully for over five years leads us to believe that we are not in error. Does the literature substantiate our confidence in this method?

M.D., Illinois.

ANSWER.—Artificial rupture of the membranes has become the accepted method of inducing labor when this procedure is indicated. Ideally, the following conditions should be present:

The pregnancy should be advanced to term or beyond it. There must be no question of cephalopelvic disproportion. The cervix should be "ripe"; that is, it should be well effaced and sufficiently softened to admit one or two fingers. The head should be engaged. When these conditions are present there is little hazard in the induction of labor. The latent period is rarely long and the labor is of average or shorter than average duration.

The real hazards occur when the indications mentioned are not present. Rupture of the membranes in the absence of a "ripe" cervix may lead to a long latent period and a prolonged and occasionally complicated labor. If the presenting part is not well engaged in the pelvis, prolapse of the umbilical cord may and does occur. The abnormal labor will increase the hazards of infection. The method is most successful at or near term and becomes less and less successful the further away from term it is attempted.

The induction of labor should be reserved for patients for whom such a procedure is indicated. Although it can be carried out with little risk in properly selected cases, it is far better to allow normal patients to go into labor spontaneously. The induction of labor for postmaturity is rarely indicated.

SNUFF HABIT

To the Editor:—A woman aged 58 wishes to break the long standing habit of using snuff. Is there any medication which may assist her in her problem?

August C. Orr, M.D., Bismarck, N. D.

ANSWER.—Whether the cessation of the snuffing habit is desired for social, esthetic, economic or hygienic reasons, the measures advised must be psychologic and environmental more than pharmacologic. The craving for nicotine may be alleviated by replacement with lobeline hydrochloride, though the lobelia addiction may be just as undesirable. The motor component of the snuff chewing habit may be replaced by that of chewing gum or candy. The use of pepper and other sternutatories instead of snuff has not met with favor. The development of unpleasant associations by giving ill smelling, ill tasting or unpleasant acting drugs such as asafetida, aloin or apomorphine with the tobacco has been suggested, as in a popular treatment for alcohol addiction. Painting the throat with silver nitrate causes a bad taste on attempting to smoke, but this effect may not be found on chewing or snuffing.

Lessening of the availability of the supply or of reminders of its use, and increase in other interests to distract attention and lessen the impulse to the use of the snuff may be of aid. Clarification and reinforcement of the conscious reasons for abandoning the habit, and encouragement of the individual to develop and display her will power in this connection may be effective.

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Control of the Smoking Habit, Queries and Minor Notes, THE JOURNAL, June 3, 1939, p. 2350.

CORONARY DISEASE DIFFERENTIATED FROM DIAPHRAGMATIC HERNIA

To the Editor:—A man aged 66 has coronary disease but is otherwise in excellent condition. What are its classic and differential symptoms compared with those of diaphragmatic hernia? Compared with the incidence of coronary disease, about what is its ratio to that of diaphragmatic hernia? What type of therapy would you regard best suited for a diaphragmatic hernia diagnosed as such in a patient as here briefly described?

C. B. Greear, M.D., Honaker, Va.

ANSWER.—The classic symptoms of coronary disease are substernal pain with radiation to the left shoulder and arm or, less frequently, to the right. There may also be radiation to the neck and jaws. The pain is usually associated with a sense of oppression. This pain is usually precipitated by exercise and particularly by exercise shortly after eating. The practical difficulty lies in the fact that there are so many variations from the classic picture. This pain or one of its variations can be differentiated from that of diaphragmatic hernia in many cases only by visualizing the hernia. In fact, it may be that the pain of diaphragmatic hernias is really due to reflex coronary constriction. It is impossible to say what percentage of coronary pain is caused by diaphragmatic hernias, but such a cause is sufficiently frequent to warrant the search for diaphragmatic hernia whenever possible. The symptom that most often arouses suspicion of diaphragmatic hernia is coronary type of pain that comes on with the patient recumbent and which is relieved when the patient assumes an upright position. X-ray examination is, however, the final diagnostic test for diaphragmatic hernia. Active treatment of such hernia is not satisfactory. In most cases coronary dilators plus palliative treatment will cause an amelioration of symptoms.

DERMATITIS FROM WEEDS OF RAGWEED GROUP

To the Editor:—A patient has a contact dermatitis from weeds. On patch testing he is sensitive to western ragweed, Santa Maria feverfew, crane's bill and burweed marsh elder. Kindly let me know in what parts of the United States he might live where all these weeds are absent or present only in small numbers.

M.D., Colorado.

ANSWER.—Western ragweed (Ambrosia psilostachya) is widely distributed over the western half of the United States. It is not abundant east of Oklahoma, Kansas and the Dakotas except perhaps in western Minnesota.

Santa Maria feverfew (Parthenium hysterophorus) is common throughout the Southern states as far west as Texas, being found in southern Missouri, southern Illinois and in the area south of the Ohio River.

Crane's bill, or wild geranium (Geranium spp.), covers a genus of some ten species, several of which are common throughout the Eastern, Northern and Central states.

Burweed marsh elder (Iva xanthifolia) is a ragweed which grows abundantly in the northern Mississippi and Missouri valleys and in many places in the intermountain states.

There is no appreciable area where all four plants are absent. Locally one might find plenty of places where over a limited area none of the plants would be present—for example, in a wooded section in the Rocky Mountain area or a seacoast locality such as Miami, Fla. Since the allergy in question involves contact with the plant it should be easy in almost any large city to avoid all four offenders. Cleveland would be free from all except crane's bill, and this would probably be found only in wooded parks or forest preserves. However, the close relationship of western ragweed to common ragweed would suggest caution in close exposure to the latter, which is, of course, widely distributed over the Eastern states.

GASTROINTESTINAL SYMPTOMS AND GRASS EATING

To the Editor:—A boy, aged 13, had vague lower abdominal discomfort. His appendix had been removed. Temperature, pulse and respiration were normal. There was some constipation and some dysuria but nothing in the urine. After three days' rest and a bland diet he was symptom free. On the morning of my last visit I saw that he had a pocket full of green grass, which, it developed, he had been in the habit of putting in his mouth. It was denied that he actually chewed it. Is there anything in grass that might produce gastrointestinal symptoms or genitourinary symptoms if the grass should be tasted or chewed?

M.D., Massachusetts.

ANSWER.—W. C. Muenscher (Poisonous Plants of the United States, New York, Macmillan Company, 1939) mentions a number of grasses as poisonous under certain conditions. These include Sorghum vulgare (sorghum), Sorghum halepense (Johnson grass) and Holcus lanatus (velvet grass, mesquite grass), which may cause poisoning as the result of the formation of prussic or hydrocyanic acid on hydrolysis.

Lolium Temulentum L. (darnel, tares, poison rye grass), widespread in the United States, contains the toxic alkaloid temuline. According to some authorities darnel is poisonous

only when infected by the fungus Endocladium temulentum. Apathy, sleepiness, giddiness, mydriasis, nausea and vomiting followed by abdominal cramps have been ascribed to darnel poisoning in human beings.

Eragrostis cilianensis (stink grass, meadow snake grass) and Stipa robusta (sleepy grass) may cause poisoning in horses, but the animals always recover.

Toxic symptoms may be produced also by poisonous weeds eaten with grass and by rusts, smuts and molds present on grass.

Most ordinary grasses such as are found on city lawns (for example, June, crab and orchard) aside from producing a bitter taste in the mouth are not harmful. Of course, if eaten in sufficient quantities, mechanical disturbances of the intestine may result. It is of interest to note that grass, either in chopped form or as tablets prepared from dried and powdered grass, may be ingested by human beings without untoward effects. Similarly the juice extracted from grass has been administered to both children and adults without ill effects.

Although the nature of the grass is not mentioned, it seems unlikely that it is a member of the poisonous group. In all probability the patient's symptoms were entirely unrelated to the tasting or chewing of grass.

PLASMA ELECTROLYTES

To the Editor:—**What are the normal limits of plasma electrolyte millimols?**

Captain, M. C., A. U. S.

ANSWER.—The total plasma electrolytes equal the sum of the positively charged cations and negatively charged anions in solution in plasma. In considering acid-base balance it is convenient to use a unit of concentration which reflects the equality between the total positive and total negative ions and permits the comparison of concentrations of different ions in units that are electrolytically equivalent. Hence in discussing plasma electrolyte concentrations the unit milliequivalent is preferable to the unit millimol. A milliequivalent equals a millimol divided by valence. Milliequivalents may be derived from milligrams per hundred cubic centimeters as follows:

$$\frac{\text{mg. per 100 cc.} \times 10}{\text{molecular weight}} = \text{millimols per liter}$$

millimols per liter × valence = milliequivalents per liter.

The following table gives the upper and lower limits of plasma electrolyte concentrations expressed as milliequivalents per liter:

	Base meq/L.		Acid meq/L.
Na^+	136.0-144.0	HCO_3^-	25.0- 27.0
K^+	4.0- 5.0	Cl	98.0-106.0
Ca^{++}	4.8- 5.2	HPO^{++}	1.8- 2.5
Mg^{++}	2.5- 3.5	SO_4^{++}	0.8- 1.2
		Organic acid	4.0- 8.0
Average total	155	Protein	14.0- 18.0
		Average total	155

IRRITATION FROM COAL TAR OR PINE TAR

To the Editor:—**I have had contact eczema dermatitis on my hands for two years. It was due to tar. Will you kindly give me information on coal tar products or products with the benzene ring.**

Alfred A. Newberry, M.D., Twin Falls, Idaho.

ANSWER.—The query is rather an indefinite one because there are at least two types of tar, coal tar and pine tar, which differ somewhat in composition. Neither of the tars is a chemical entity; they consist of a great many hydrocarbons.

A great many chemicals are derived from tar either directly or by chemical combination.

Many of the chemicals in tar will irritate the skin and many of them will sensitize the skin. Some of them are photosensitizers.

It would be desirable to find which of the ingredients of tar cause the trouble. This can be done by performing patch tests, first with coal tar itself to verify the diagnosis, second with the coal tar distillates and third with the basic chemicals found in the particular distillates which show the strongest reactions from the patch tests.

References:

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FUNCTIONS OF VERTEBRAE AND ARTICULATING PROCESSES

To the Editor:—**Following a fall from a horse and in turn having the horse fall on me, I received a slight fracture of the body of the fourth lumbar vertebra; that is, the superior lip was pushed down approximately an eighth of an inch, slivering the bone parallel and under the anterior longitudinal ligament. The injury has been remarkably free from any pain or discomfort, which is more than I can say for the treatment that has been directed toward keeping my lumbar spine in a mild degree of hyperextension. I have been struck with the fact that all of my colleagues seemed to be particularly obsessed with an assumption that the bodies of the vertebra are principally supporting blocks to the upright position or, rather, erect posture. My contention is that all of the antigravitational force is centered in the articular processes at the root of the vertebral arches and is balanced antigravitationally in the supraspinal ligaments evolving the anticlinical vertebra; in other words, the bodies of the vertebrae and the intravertebral disks are progravitational, reducing the function of the body and the intravertebral disk to a cushioning, counterbalancing and shock absorbing rather than supporting. Sir Samson Wright in Applied Physiology discusses this question in his chapter on muscle tone and regulation of posture from the standpoint of muscles and nerves but does not correlate this with any physical structure of the bones. To reexamine the foregoing assumption, what are some of the recent opinions as to the importance of the bodies of the vertebra in maintaining the erect posture?**

H. D. Allen Jr., M.D., Milledgeville, Ga.

ANSWER.—There is a difference of opinion as to just what the total functions of the articulating processes at the bases of the vertebral laminas are. The probabilities are that they have little to do with the actual weight bearing. Weight bearing most probably is taken care of through the bodies of the vertebrae and the intervertebral disks. The chief function of the articulating processes is that of preventing a forward slipping of the upper vertebra on the one below.

In neurosurgery it is often necessary to perform a wide laminectomy in which the articulating facets (articular processes) are removed on both sides and the patients get along well. The old question comes into prominence here as to whether or not ligaments give the most support or the muscles. Both are essential. The spinal bony column is made up of a number of separate bones, one on top of the other, held together by their contour and strong reinforcing ligaments. In a way the spine can be likened to a tent pole and the muscles to the guy ropes that hold the pole erect.

Clinically, it has long been known that a slight compression fracture along the anterior border of a vertebra may give little or no discomfort, and treatment in such cases by hyperextension is not necessary.

FOCAL (ESPECIALLY DENTAL) INFECTION AND NEPHROLITHIASIS

To the Editor:—**What are the possible relationships between infections, particularly pyorrhea, and nephrolithiasis? Two articles have come to my attention, one in the January 1943 issue of the Merck Report by G. de Leo, M.D., urologist, Columbus Hospital, New York, and an article which appeared in the *Dental Cosmos* for November 1931 entitled "Dental Focal Infection as an Etiological Factor in Diseases of the Genitourinary System," by Herbert Sugar, M.D., Los Angeles. A question has recently arisen in a case in which there was a definite history of nephrolithiasis from a period of over eighteen years which eventuated in the surgical loss of one kidney. Pyorrhea preceded and was coincident with attacks of renal colic and passage of gravel for the first three or four years. Specifically, could this pyorrhea be considered as having an etiologic bearing on the kidney condition?**

M.D., Montana.

ANSWER.—Many factors are involved in the etiology of nephrolithiasis. Infection of the urinary tract is undoubtedly important in recurrent stone formation, particularly when urea splitting organisms are present, for example Proteus vulgaris, Escherichia coli, staphylococci, Bacillus pyocyaneus, Hemophilus influenzae and certain streptococci. There are various possible sources of origin for these bacteria, among which the colon must be given a prominent role.

Ever since the experimental production of renal calculi in dogs by streptococcic infection of devitalized teeth (Rosenow and Meisser), many clinicians have accepted the theory of focal dental infection, including pyorrhea, as a factor in nephrolithiasis. Search of the literature does not reveal significant factual support for this view. Ordinary statistical studies prove nothing in view of the high incidence of pyorrhea and its resultant coincidence with many other diseases. Another difficulty is the fact that the bacteria found in dental infection are usually streptococci, while the organisms found in the urine of individuals with stones are likely to be colon or proteus bacilli or staphylococci (Keyser). However, streptococci have been found by means of the Gram stain in a large proportion of calcific plaques on renal papillae (E. C. Rosenow Jr.). The significance of this observation is highly debatable apart from the fact that no deduction is possible regarding the origin of the bacteria in this series of cases.

It would therefore seem unwarranted to conclude that the patient's pyorrhea had an etiologic bearing on his nephrolithia-

sis. On the other hand, one could not draw the opposite conclusion in this specific instance. Carefully controlled clinical observations, early in the course of kidney stone formation, are badly needed.

References:

Rosenow, E. C., and Meisser, J. G.: The Production of Urinary Calculi by the Devitalization and Infection of Teeth in Dogs with Streptococci from Cases of Nephrolithiasis, *Arch. Int. Med.* **31**: 807 (June) 1923.
Keyser, L. D.: The Relationship of Urinary Infections to Recurrent Calculi, *J. Urol.* **31**: 219 (Feb.) 1934.
Higgins, C. C., and Mendenhall, E. E.: Factors Associated with Recurrent Formation of Renal Lithiasis, *ibid.* **42**: 436 (Sept.) 1939.
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DESTRUCTIVE LESION OF TERMINAL INTERPHALANGEAL JOINT

To the Editor:—**A patient aged 48 has had swelling and discharge from the right middle finger for the past six months. This discharge has the appearance of joint fluid. An x-ray film shows that there is rather extensive destruction of the terminal interphalangeal joint of the right middle finger. There is also evidence of some slight bony destruction in the opposing bony surfaces. This involves both the terminal and the middle phalanx. There is no evidence of any osteomyelitis. The findings in this case are quite typical of infectious arthritis. The condition is suggestive of osteoperiositis albuminosa. With these findings, could you suggest the best method of treating this condition?**

R. V. Jolin, M.D., Grand Rapids, Minn.

ANSWER.—Tuberculosis of a single interphalangeal joint is more common than is the condition referred to as osteoperiostitis albuminosa. Destruction of a finger joint without new bone formation in the region should be considered tuberculosis until proved otherwise. A biopsy is indicated. If the diagnosis is confirmed, amputation of the distal phalanx will give the most certain and most prompt recovery of use of the hand. The alternative method of treatment is long continued splinting of this finger in a position of slight flexion. It should be remembered, however, that a fused interphalangeal joint is a much more serious handicap than is the loss of the distal phalanx of a finger.

PRESERVATION OF LIQUID PLASMA

To the Editor:—**How long can properly processed liquid plasma be safely kept on a shelf at room temperature and at average refrigerator temperature? Also how often should such plasma be cultured for sterility?**

M.D., District of Columbia.

ANSWER.—The preservation of plasma in the liquid state should be avoided as much as possible.

In any case liquid plasma should not be preserved at refrigerator temperature, because of massive irreversible flocculation. If very thorough sterility tests have been performed, the expiration date for liquid plasma kept at room temperature (15 to 30 C.) has been set at one year by the National Institute of Health.

It is not necessary to repeat the sterility tests if proper cultural studies were done at the time of pooling the plasma and if the material was not subsequently exposed to contamination.

COCCYGEAL INJURY AND TRAUMATIC ARTHRITIS

To the Editor:—**A man aged 71 fell out of bed and struck on the lower part of his spine. Considerable pain and disability followed, and an x-ray examination showed a fracture of the last bone of the coccyx—not straight across the bone but slanting. A few weeks after the original injury tenderness developed in one of the lower lumbar vertebrae on pressure; x-ray examination showed no signs of fracture or dislocation, but there was evidence of arthritis. The patient's general condition is fairly good, but it is difficult for him to get about, his legs feeling weak and a certain numbness being present. Bowel and bladder functions are good and with the aid of vitamin B_1 his appetite is satisfactory. I shall appreciate any advice or suggestions for treatment of this patient. Can you give any estimate as to the length of disability?**

F. S. Spearman, M.D., Williams, Ariz.

ANSWER.—The fact that the pain is in the lower lumbar area would indicate it is not a coccygeal injury that is causing the pain. The discomfort may be due entirely to the arthritis in the lumbar part of the spine, the fall being the contributing factor, causing a traumatic arthritis on top of the old. There is no specific treatment but rest, not necessarily to the point of rest in bed but to the point of moderation in activities, and application of heat to the affected area, preferably radiant heat, along with gentle massage, will do as much as anything. In a man of this age metastatic cancer must be considered, and careful examination of the prostate and inquiry as to gastrointestinal symptoms should be carried out. The length of disability is difficult to estimate, but if traumatic arthritis on top of old osteoarthritis is the basis, the patient should experience considerable improvement in a few weeks.

REACTION TO PITRESSIN TANNATE

To the Editor:—**A woman aged 40 has diabetes insipidus. I am giving her pitressin tannate into her gluteal muscle. Six months ago she had a reaction. Yesterday she had another reaction from the injection. These reactions came on immediately after taking the injection. I did not see her immediately, but at the time I saw her she had a fever, felt cold and had a feeling of constriction in her chest. Her blood pressure was normal. A small injection of epinephrine increased her discomfort. I gave her a small amount of morphine, after which she felt warm and had some relief. I feel sure this was not a hysterical manifestation, as her temperature was almost 102 F. It seemed to me to be a foreign protein reaction. She remained ill for twenty-four hours, at the end of which time she seemed completely recovered. She is taking these injections at forty-eight hour intervals. Can you give me any more information about this type of reaction, the probability of its recurrence and the probability of its being fatal? What is the treatment?** **M.D., Iowa.**

ANSWER.—The literature relating to the use of pitressin tannate for the treatment of diabetes insipidus is listed below. Reaction to this type of treatment has not been reported. The best suggestion to follow would be to abandon this type of treatment in this particular case and to institute the use of posterior pituitary powder by nasal insufflation. A small amount of the powder, about that which rests on the end of a knife blade or nail file, is simply placed in a tube with atomizer bulb and blown into the nose. This is a much less wasteful method than having the patient attempt to introduce it digitally or to sniff it from a paper. Most patients are controlled with two administrations, one in the morning and one at bedtime. Some patients who do not mind the polyuria and polydipsia during the daytime use it only at night. This method is by far the least expensive method and the one which most patients prefer. It is interesting that 4 of the 8 patients mentioned by Blotner "have discontinued the use of pitressin tannate in oil because they can take pituitary intranasally and avoid injections."

References:

Blotner, Harry: Pitressin Tannate in Oil in the Treatment of Diabetes Insipidus, THE JOURNAL, July 25, 1942, p. 995.
Greene, J. A., and January, L. E.: Diabetes Insipidus Treated by Subcutaneous Administration of Suspension of Pitressin Tannate in Oil, *ibid.*, Oct. 5, 1940, p. 1183.
Souders, C. R.: Treatment of Diabetes Insipidus by Pitressin Tannate in Oil, *Lahey Clin. Bull.* **2**: 244 (April) 1942.
Stephens, D. J.: Pitressin in Oil: Prolonged Antidiuretic Effect in Experimental and Clinical Diabetes Insipidus, abstr. *J. Clin. Investigation* **20**: 463 (July) 1941.
Thorn, G. W., and Stein, K. E.: Pitressin Tannate Therapy in Diabetes Insipidus, *J. Clin. Endocrinol.* **1**: 680 (Aug.) 1941.

INTRACTABLE INSOMNIA

To the Editor:—**A woman aged 66 insists that she is unable to sleep. I have tried everything I can think of or can read about without success. I know of no reason why she cannot sleep. Any advice that you can give me will be appreciated.** **M.D., Ontario.**

ANSWER.—Intractable insomnia is often extremely difficult to treat. It is important, if possible, to get at the cause of the insomnia; diseases of the central nervous system are especially liable to produce insomnia, and frequently insomnia may be of psychogenic origin. It is most important, therefore, to eliminate organic causes for the insomnia by careful examination of the central nervous system and to investigate possible psychogenic origins. If anything is found, the treatment should be directed toward the disease process causing it. For the simpler types of insomnia without serious organic or functional causes, the following references may be suggested:

Alvarez, W. C.: Help Your Doctor to Help You When You Have Insomnia, New York, Harper & Brothers, 1942.
Jacobson, Edmund: You Can Sleep Well, New York, McGraw-Hill Cook Company, 1938.

APPLICATION OF HEAT OR CHEMICALS TO SKIN OF PATIENT TREATED BY X-RAYS

To the Editor:—**A patient had intensive x-ray treatment of the front, back and outer hip-thigh regions, with considerable skin reaction. She applied dry heat to the outer aspect of her thigh (in an area treated with x-rays) for the relief of local pain. The x-ray man told her not to do that, for the heat thus locally applied over an irradiated area would much increase the local x-ray skin reaction, making it much worse. Is that true or at least enough true so that external heat should not be used?**

Stuart B. Blakely, M.D., Binghamton, N. Y.

ANSWER.—It is usually inadvisable to use any type of irritation, whether thermal or chemical, on the skin of a patient subjected to x-ray therapy. It is not unusual to have a skin reaction greatly exaggerated following the application of local heat even though the amount of x-rays delivered to the skin is not sufficient to cause a definite skin reaction. It is believed that a patient receiving x-ray therapy should not have heat or irritating chemicals applied to the skin.